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PROPHYLAXIS OF RICKETS IN PREMATURE INFANTS WITH VITAMIN D MILK

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The problem of the reenforcement of milk with vitamin D has assumed increasing importance in recent years, since this type of milk in its various forms is being marketed widely throughout the country. In spite of numerous studies, pediatricians and others having to do with the feeding of infants are in doubt as to the extent to which this type of milk can protect a growing infant from rickets. The majority of studies have dealt with the problem of curing rickets already established. Up to the present, few studies have been reported on the prophylactic potency of this type of antirachitic agent.

A comprehensive review of the reports of clinical experiences with vitamin D milk published prior to October 1934 was made by Bunker and Harris.[1] They expressed the opinion that irradiated milk and milk from cows fed irradiated yeast had each proved to be valuable both in the cure and in the prevention of rickets when employed in the amounts used and in the manner usually applied with ordinary milk in the feeding of infants. In the experiments reviewed no constant difference had been demonstrated in the relative efficacies of these two types of milk in terms of potency according to rat unit equivalents. They indicated a number of problems remaining unsolved: the special requirements of very young infants in respect to antirachitic factors; the minimum antirachitic potency of milk required for complete protection of all infants, and the quantity of vitamin D needed to insure the greatest rapidity of the healing process.

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1. Bunker, J. W. M., and Harris, R. S.: The Clinical Status of Vitamin D Milks, New England J. Med. **211**:1140 (Dec. 20) 1934.

Jeans and Stearns [2] in 1934 studied the effectiveness of vitamin D in infants in relation to its source. They tested three different types of milk: (1) irradiated evaporated milk, (2) nonirradiated evaporated milk fortified with the unsaponifiable fraction of cod liver oil (Zucker concentrate) and (3) nonirradiated evaporated milk to which plain cod liver oil was added. The irradiated product when diluted to the concentration of whole milk contained 50 Steenbock (135 U.S.P.[2a]) units of vitamin D per quart (946 cc.) of reconstituted milk; the other products were adjusted to the same potency of vitamin D by dilution of the milk fortified with the Zucker concentrate with ordinary evaporated milk and by the appropriate choice of the amount of cod liver oil added. The youngest infants received 22 (59.4 U.S.P.) units daily, but by the age of 16 weeks all received 50 (135 U.S.P.) units daily. Seven infants ranging from 5 weeks to 1 year of age were given the diets including the three types of milk in rotation for a period of six weeks each. The retention of calcium observed in the group as a whole averaged about 10 mg. per kilogram of body weight and was lower for any given intake of milk than the retention of calcium observed in previous experiments with infants given 125 (337.5 U.S.P.) units of vitamin D per day. No clinical or roentgenographic evidence of rickets was observed in any of these infants, but the rate of growth in length was not as good as in the group previously studied.

Wyman, Eley, Bunker and Harris [3] studied 6 infants (2 of them premature) with active rickets. The infants were hospitalized and fed from 26 to 32 ounces (from 765 to 944 cc.) of either irradiated milk containing 50 Steenbock (135 U.S.P.) units or milk from cows fed irradiated yeast containing from 60 to 65 Steenbock (from 162 to 175 U.S.P.) units per quart. These infants showed healing of the rickets within four weeks. Wyman and his associates did not note a difference between the efficacy of the two types of milk, unit for unit.

Gerstenberger, Horesh, Van Horn, Krauss and Bethke,[4] in a comparative study of the antirachitic value of irradiated milk and milk produced by cows fed irradiated yeast, studied 13 rachitic infants (all Negroes except one). After a preliminary period of observation, during

2. Jeans, P. C., and Stearns, G.: Effectiveness of Vitamin D in Infancy in Relation to the Vitamin Source, Proc. Soc. Exper. Biol. & Med. **31**:1159 (May) 1934.

2a. Throughout this paper U.S.P. Unit refers to the U.S.P.X unit as revised in 1934.

3. Wyman, E. T.; Eley, R. C.; Bunker, J. W. M., and Harris, R. S.: A Comparison of "Yeast Milk" and Irradiated Milk in the Treatment of Infantile Rickets, New England J. Med. **212**:257 (Feb. 7) 1935.

4. Gerstenberger, H. J.; Horesh, A. J.; Van Horn, A. L.; Krauss, W. E., and Bethke, R. M.: Antirachitic Cow's Milk: A Comparative Study of Antirachitic Value of Irradiated Cow's Milk, and of Milk Produced by Cows Fed Irradiated Yeast, J. A. M. A. **104**:816 (March 9) 1935.

which the activity of the rachitic process was established, the infants were given one or the other of the experimental foods, the daily diet containing either 480 or 720 cc. of milk. The authors concluded that for rachitic infants there is no practical difference between the antirachitic efficacy of the two types of milk when the same amount of antirachitic factor is administered, as represented by an identical number of rat units per day. The antirachitic factor in both types of milk was 40 Steenbock (108 U.S.P.) units per day; this amount produced satisfactory healing in the blood in from forty-nine to sixty-one days and in the bones in from ten and a half to eleven weeks. In another experiment milk from cows fed irradiated yeast assayed at 27.5 Steenbock (74 U.S.P.) units per day also effected satisfactory healing in the blood and in the bones. However, the period required to bring about this result in the blood averaged one hundred and eighteen days and in the bones twenty-one weeks. Gerstenberger and his associates expressed the opinion that the dose of 27.5 (74 U.S.P.) units per day is close to the actual minimum amount required for the ultimate healing of active rickets. These authors sounded a note of warning against drawing conclusions as to the relative antirachitic effectiveness of cod liver oil and antirachitic milk. They criticized Kramer and Gittleman's [5] statement that vitamin D milk is the most effective antirachitic agent.

Of the questions raised by Bunker and Harris, the most important would seem to be whether by any means at one's command one can completely protect the very young infant from rickets during the period of active growth. It has been shown that there is a definite relationship between the rate of growth in the infant and the amount of vitamin D needed to protect him. Therefore the prevention of rickets during the early months of an infant's life when growth is most rapid is a more severe test of an antirachitic factor than the cure of rickets several months later when the rate of growth is much less. Does fortified milk give adequate protection during this early period, or is additional vitamin D necessary, and if so, how much? The significance of this question is emphasized by the fact that during the early months, when the need for vitamin D is probably greatest, the infant is able to take relatively less milk than during the middle and later months of the first year. Few studies have been reported on the prophylactic value of vitamin D milk in very young infants, and to the present time none have been carried out in which the administration of vitamin D milk was begun at birth. In 1931 Hess and his associates [6] made a study of the comparative antirachitic potency of the milk of cows fed either irradiated

5. Kramer, B., and Gittleman, I. F.: Vitamin D Milk in the Treatment of Infantile Rickets, New England J. Med. **209**:906 (Nov. 2) 1933.

6. Hess, A. F.; Lewis, J. M.; MacLeod, F. L., and Thomas, B. H.: Antirachitic Potency of the Milk of Cows Fed Irradiated Yeast or Ergosterol: A Clinical Test, J. A. M. A. **97**:370 (Aug. 8) 1931.

ergosterol or irradiated yeast. Two groups of 25 infants each received milk from cows fed viosterol, and two similar groups received milk from cows fed irradiated yeast. The infants in the latter two groups ranged in age from 1½ to 6 months and received an average of 750 cc. of milk from cows fed irradiated yeast daily. For one group of 25 infants this milk contained 160 Steenbock (430 U.S.P.) units per liter, and for the other group of 25 the milk contained 80 Steenbock (215 U.S.P.) units per liter. Hess and his associates found that in both groups rickets was prevented, except in its minor clinical manifestations, and that rickets visible in roentgenograms did not develop. As a prophylactic study this work was inconclusive, however, because at the outset 13 infants had rickets visible in roentgenograms and 36 had some evidence of clinical rickets. Also, 33 of the infants had received cod liver oil prior to the beginning of the experiment. In order to evaluate prophylactic studies properly the antirachitic factor should be administered in the neonatal period and should be continued through the fifth or sixth month of life. We believe that the failure to observe these conditions subjects the work of Hess and his co-workers to criticism and further renders their findings inconclusive.

Drake, Tisdall and Brown [7] in 1934, in a study of the relative antirachitic value of cod liver oil, viosterol and irradiated milk, observed 529 infants. From 20 to 40 ounces (from 590 to 1,180 cc.) of irradiated vitamin D milk containing 35 Steenbock (94 U.S.P.) units per 20 ounces was given daily to 141 infants, ranging in age from 3 weeks to 8 months at the initial examination. The milk was administered over a period of five winter months. For comparison 65 infants were not given vitamin D. The infants were divided into two groups, those less and those more than 4 months of age at the beginning of the experiment. The effectiveness of such feeding in the prevention of rickets in both groups, as evidenced by roentgen study, and the comparison with the group which did not receive an antirachitic factor are shown in tables 1 and 2.

While moderate or marked rickets did not develop in any infant, it was found that 20 ounces of irradiated vitamin D milk daily is insufficient for the complete protection of infants under 4 months of age. Drake, Tisdall and Brown pointed out that this is due to the inability of the young infant to consume an amount of milk adequate for protection and that therefore it is desirable during the early months of life to supplement the irradiated milk with some other antirachitic substance.

Since the tendency to the development of rickets varies directly with the rate of growth of bone, it is well recognized that the minimal protective dose of vitamin D must be relatively large during the early

7. Drake, T. G. H.; Tisdall, F. F., and Brown, A.: A Study of the Relative Antirachitic Value of Cod Liver Oil, Viosterol, and Irradiated Milk, Canad. M. A. J. **31**:368 (Oct.) 1934.

months of life and must be even larger in the first postnatal months of life of a thriving premature infant. In an earlier study [8] two of us described our efforts to prevent rickets by the administration of viosterol to 13 premature infants. With the preparation and dosage used we were not completely successful. In a control group of 22 infants, who did not receive antirachitic therapy, rickets of a more severe type developed than was observed in the group of infants who received

TABLE 1.*—*The Effectiveness of Irradiated Milk in the Prevention of Rickets as Evidenced in Roentgenograms* †

Age	Total Number of Patients	Very Slight Rickets	Mild Rickets	Moderate and Marked Rickets
Under 4 months at initial examination				
No vitamin D	31	8	6	4
1 pint (20 ounces) of irradiated milk daily	38	13	3	0
From 4 to 8 months at initial examination				
No vitamin D	34	6	4	1
1 pint (20 ounces) of irradiated milk daily	33	3	3	0

* This table is reprinted with slight modifications, from Drake, Tisdall and Brown.[7]
† The figures are based on the maximum degree of rickets observed at any time subsequent to the initial examination.

TABLE 2.*—*The Effectiveness of More Than One Pint of Irradiated Milk in the Prevention of Rickets as Evidenced in Roentgenograms* †

Age	Total Number of Patients	Very Slight Rickets	Mild Rickets	Moderate and Marked Rickets
Under 4 months at initial examination				
No vitamin D	31	8	6	4
Over 1 pint (from 20 to 40 ounces) of irradiated milk daily	9	5	1	0
From 4 to 8 months at initial examination				
No vitamin D	34	6	4	1
Over 1 pint (from 20 to 40 ounces) of irradiated milk daily	61	6	1	0

* This table is reprinted with slight modifications, from Drake, Tisdall and Brown.[7]
† The figures are based on the maximum degree of rickets observed at any time subsequent to the initial examination.

viosterol. In further studies now in progress we are giving another preparation and another dosage of viosterol to one group of premature infants; to another group irradiated evaporated milk is being given as the sole antirachitic factor. The study reported here was undertaken to determine how great a degree of protection could be afforded the premature infant by the administration of vitamin D milk [9] without an added antirachitic substance.

8. Davidson, L. T., and Merritt, K. K.: Viosterol in the Prophylaxis of Rickets in Premature Infants, Am. J. Dis. Child. **48**:281 (Aug.) 1934.

9. This milk was supplied by the Walker-Gordon Company, Plainsboro, N. J.

METHOD OF STUDY

The preparation used was the same as that labeled vitamin D milk offered for sale in the city of New York and was delivered to the infants' homes by the company furnishing it. The milk was produced at the company's dairy in New Jersey. The herd comprised about 50 per cent Holstein, 20 per cent Guernsey, 15 per cent Jersey and 15 per cent Brown Swiss cows. The grain mixture for the cows was made up of ground corn, oats, wheat bran, corn gluten feed, linseed meal, brewer's grains, coconut-oil meal, irradiated yeast and salt. The remainder of the ration consisted of machine-dried alfalfa hay, corn silage and dried beet pulp. The cows were kept on the same ration throughout the year and received no pasture. As a rule the cows were kept indoors, but occasionally they were turned out into lots for a few hours on a pleasant day.

The yeast [10] which these cows received was assayed at the Fleischmann laboratories and contained 933 Steenbock (2,520 U. S. P.) units per gram. The yeast was incorporated, as stated previously, in the grain mixture of the cows. Wilson and Hardenbergh [11] of the Walker-Gordon Laboratory stated that this manner of mixing insures automatic and regular feeding of the yeast and provides automatic adjustment of the amount fed to the requirements of the individual cow, since it is good dairy practice to feed grain in proportion to the amount of milk produced. It is known that the requirement of yeast for a given potency of the milk is proportional to the amount being produced. This can be calculated from a formula, which takes into account the amount of milk produced by the herd, the amount of grain fed the herd and the average daily production per cow. It has been observed that the factor governing the vitamin D potency of the milk is the total amount of milk secreted daily and not the total amount of butter fat. Cows with a high rate of production are more efficient in transferring vitamin D from their feed to their milk than cows with a low rate of production. A cow producing 30 pounds (13.6 Kg.) of milk a day requires in the daily ration approximately 4.3 ounces (133.73 Gm.) of yeast of the assay mentioned previously to produce milk containing 160 (432.7 U. S. P.) units of vitamin D per quart. After the feeding of yeast is started, it takes about twenty days for the cow's milk to reach maximum potency. Frequent bio-assays of the vitamin D milk were made at the Fleischmann laboratories, totaling eight assays during the period of our study. The results of the assays were as follows:

Month 1934	Results of Bio-Assays
January	Slightly more than 160 Steenbock (432 U. S. P.) rat units per quart
March	160 Steenbock (432 U. S. P.) rat units per quart
April	More than 170 Steenbock (459 U. S. P.) rat units per quart
May	More than 170 Steenbock (459 U. S. P.) rat units per quart
June	160 Steenbock (432 U. S. P.) rat units per quart
November	Less than 160 Steenbock (432 U. S. P.) rat units per quart
December 1935	Less than 160 Steenbock (432 U. S. P.) rat units per quart
January	160 Steenbock (432 U. S. P.) rat units per quart

All infants included in this study except 1 were born in the Sloane Hospital for Women, where they remained under our observation for varying periods until they reached a weight of 2,250 Gm. One infant (J. V.), born at home, was

10. The yeast was produced by the dry yeast department of Standard Brands, Inc.

11. Hardenbergh, J. G., and Wilson, L. T.: Production of Antirachitic Milk by the Feeding of Dairy Cattle, Am. J. Pub. Health **23**:230 (March) 1933.

admitted to the Babies Hospital at the age of 11 days. When they were discharged the infants were referred to a follow-up clinic, where they were seen every two weeks or oftener during the experiment. All clinical observations and records were made by one of us. It was believed that the infants who did not receive antirachitic therapy in a previous study [8] might serve for comparison, so that further controls were unnecessary.

Frequent visits were made to the infants' homes by a social worker to insure that instructions given at the clinic were followed. Although a daily record of the intake of milk was not kept in the home, the mother was questioned closely on each visit as to the exact number of ounces of milk used in making the formula and whether the infant was refusing any appreciable amount, was vomiting or was having diarrhea. Because the infants were premature, it seemed unwise to give them vitamin D milk until after they had received breast milk or evaporated milk (nonirradiated) long enough to demonstrate their growth impulse. This preliminary period varied from five to thirteen days. One infant received S. M. A. from the first to the eleventh day of this preliminary period. The experimental formula was started with the vitamin D milk representing about 40 per cent of the total volume and was rapidly increased to undiluted milk, according to the

TABLE 3.—*The Daily Intake of Milk and Vitamin D of Premature Infants*

Age, Months	Average Daily Intake of Milk, Cc.	Average Daily Intake of Vitamin D, U. S. P. Units
1	392	168
2	630	267
3	710	305
4	824	353
5	931	400
6	947	407

infant's tolerance, the caloric intake being kept at approximately 130 calories per kilogram. The average daily intake of milk and of vitamin D at the various months is shown in table 3.

As the object of this study was to determine the degree of protection against rickets afforded infants by vitamin D incorporated in the milk, the regimen as regards both feeding and management was arranged to conform to the usual practice in the feeding of infants. Solid food was given as follows: cereal at the fourth or fifth month and vegetables at the fifth or sixth month. Egg yolk, representing a small amount of added vitamin D, was given to only 3 infants before the fifth month. It was given to 1 infant at the fourth month and to 2 other infants at 4¾ months of age. We do not think that this factor had an appreciable antirachitic effect in this experiment.

As in our previous study, the mothers were instructed to keep the infants outdoors but were not told to give them sun-baths without clothes.

Roentgenograms of the forearms and wrists were made bimonthly from birth to 4 months of age and then monthly through the sixth month. The roentgenographic technic was as follows: distance, 38 inches (96.5 cm.); time of exposure, one-sixth second; milliamperes, 60, and kilovolts, 52.

The serum calcium and the inorganic phosphorus content were determined monthly throughout the experiment. Values for serum calcium and inorganic phosphorus at birth were determined in a previous study,[8] and a table of our observations and those of others may be found in that article.

TABLE 4.—*Observations on Eleven Premature Infants Receiving Vitamin D Milk*

Case	Name	Race	Birth Weight, Gm.	Birth Length, Cm.	Date of Birth	Age, Mo.	Clinical Data: Weight, Gm.	Rosary	Harrison's Groove	Changes in Epiphyses	Changes in Bossae	Craniotabes	Blood Chemistry: Calcium, Mg. per 100 Cc. of Serum	Inorganic Phosphorus, Mg. per 100 Cc. of Serum	Calcium, Phosphorus Product	Total Daily Intake of Vitamin D, U.S.P. Units	Daily Intake of Vitamin D, Units per Kg. of Body Weight	Roentgenograms, Degree and Stage of Rickets
1	F. B.	White	2,060	41.5	5/15/34	1	2,160	..	..	..	..	..	10.9	7.1	78	116	52	E
						2	3,345	..	..	..	..	..	11.1	7.0	77	215	65	E
						3	4,280	+	+	..	..	..	....	....	..	258	60	E
						4	5,160	..	..	..	..	..	11.9	7.9	94	282	55	B_1
						5	6,080	..	..	..	..	..	11.7	6.9	81	430	70	B_1
						6	6,470	..	..	..	..	..	....	....	..	430	66	C_1
2	G. H.	White	2,270	46.0	6/21/34	1	2,740	..	..	..	..	+	12.2	6.2	76	202	75	E
						2	3,980	+	..	..	..	..	10.2	6.9	70	322	80	E
						3	4,680	++	+	+	..	..	11.5	7.6	87	344	73	E
						4	5,670	+	+	..	..	..	11.9	7.6	90	344	60	E
						5	5,800	+	..	..	+	..	11.5	6.2	71	344	59	E
						6	6,400	..	..	..	..	..	11.7	6.5	76	357	55	E
3	F. K.	Negro	1,750	42.0	7/10/34	1	2,120	..	..	..	..	..	10.9	7.1	77	145	70	E
						2	3,330	..	..	..	..	..	11.7	6.9	81	282	85	B_1
						3	4,200	+	+	..	..	..	11.9	6.6	79	282	67	B_1
						4	4,340	..	..	..	..	..	11.5	7.6	87	430	100	B_1
						5	4,850	++	++	+	+	..	11.5	6.2	71	430	90	B_1
						6	5,230	++	++	+	+	..	....	....	..	430	82	B_1
4	F. L.	White	2,280	45.5	3/ 1/34	1	2,920	..	..	..	..	..	10.9	6.6	72	215	75	E
						2	4,000	..	..	..	..	..	11.7	6.6	77	322	80	E
						3	4,650	..	..	..	..	..	....	....	..	344	74	D
						4	5,390	..	+	..	..	..	11.3	6.0	68	344	63	B_1
						5	5,770	..	..	..	..	..	11.1	5.8	64	387	67	B_1
						6	6,660	+	..	..	..	..	11.3	6.4	72	387	57	B_1
5	R. M. [1]	White	2,260	45.0	3/19/34	1	2,730	..	..	..	..	..	11.3	6.9	88	145	54	E
						2	4,170	+	..	..	+	..	12.2	7.8	95	322	76	D
						3	5,760	+	..	..	..	..	11.9	8.4	100	344	60	E
						4	6,690	..	..	..	..	..	12.2	6.4	78	430	64	E
						5	7,510	.	..	..	..	..	12.2	6.1	74	430	57	E
						6	8,390	.	..	..	+	..	....	..	..	430	50	E

6	R. M. [2]	White	2,020	47.0	2/14/34	1	3,000	..	..	..	..	..	11.3	7.0	79	245	81	E
						2	3,970	..	..	+	..	.	11.1	7.4	82	322	80	D
						3	4,900	..	..	..	..	..	11.3	7.6	86	344	70	B_1
						4	5,980	++	..	..	..	..	11.7	7.1	83	404	67	B_1
						5	6,500	+	..	+	+	..	11.3	7.1	80	430	66	B_1
						6	6,920	+	..	..	..	..	....	...	..	430	62	C_1
7	E. T.	Negro	2,010	45.5	8/21/34	1	2,330	..	..	..	..	..	11.1	7.4	82	145	63	E
						2	3,180	..	..	..	..	..	11.1	6.4	71	202	63	E
						3	4,340	..	..	..	..	..	11.9	7.0	83	282	65	B_1
						4	5,130	..	..	..	..	..	11.9	7.4	88	335	62	B_1
						5	5,970	..	..	..	..	..	11.1	...	..	404	67	B_1
						6	6,700	..	..	..	..	..	11.6	6.9	80	404	60	C_1
8	C. T.	Negro	1,850	43.0	1/ 3/34	1	2,210	..	..	..	..	..	10.2	7.7	79	159	70	E
						2	3,560	..	..	..	..	..	8.7	4.5	39	236	66	D
						3	4,530	..	..	..	..	..	8.9	5.6	50	300	70	B_1
						4	5,100	..	..	..	..	..	11.1	7.5	83	292	57	B_2
						5	6,550	..	..	+	..	..	11.7	6.5	76	258	40	C_1
						6	7,330	..	+	+	..	..	11.5	6.5	75	322	44	C_1
9	J. V.	White	1,418	42.0	7/24/34	1	2,010	..	..	..	..	..	11.1	7.0	78	129	63	E
						2	3,050	..	..	..	..	..	11.1	6.3	70	219	73	A_1
						3	3,640	..	..	..	..	..	11.5	6.9	79	258	70	A_1
						4	4,100	..	..	..	+	..	11.7	6.4	75	322	80	A_1
						5	5,050	..	..	..	..	..	11.7	7.6	89	430	86	B_1
						6	6,150	..	..	..	..	..	11.5	7.8	90	430	70	B_1
10	P. Y.	White	1,890	43.0	12/ 9/33	1	2,530	..	..	..	..	..	11.5	7.0	81	180	70	E
						2	3,020	..	..	..	..	+	11.7	5.9	69	253	84	E
						3	3,970	+	..	..	++	..	10.2	5.8	59	300	75	D
						4	4,540	+	..	..	++	..	11.1	6.8	75	348	77	B_1
						5	5,250	+	..	++	++	..	11.7	6.3	74	430	83	B_1
						6	5,820	..	..	+	++	..	....	...	..	430	72	C_1
11	M. Y.	White	2,170	44.0	12/ 9/33	1	2,450	..	..	..	..	..	11.7	7.4	87	180	60	E
						2	3,030	..	..	..	+	+	11.3	6.5	73	245	80	D
						3	4,260	++	..	..	++	..	10.9	7.0	76	300	70	B_1
						4	4,750	++	..	..	++	..	10.7	6.9	74	360	76	B_1
						5	5,530	+	..	++	++	..	....	6.6	..	430	78	B_1
						6	6,200	+	..	+	++	..	....	...	..	430	70	C_1

OBSERVATIONS

Clinical Considerations.—The same criteria for the presence of rickets were applied to this group of infants as we used in the group studied previously. Table 4 shows the prevalence and severity of clinical rickets in the 11 infants studied. Negative clinical findings are represented by a blank space rather than by a zero. Positive clinical findings are represented in the order of severity on the scale of +, ++, +++ and ++++. There was in general very little rachitic involvement clinically, in contrast to that noted in the control group previously studied. One infant (F. K.) had a moderate rosary and a Harrison groove between the fifth

TABLE 5.—*The Values for Serum Calcium for Premature Infants Receiving Vitamin D Milk*

Patient	Calcium per 100 Cc. of Serum, Mg.					
	1 mo.	2 mo.	3 mo.	4 mo.	5 mo.	6 mo.
F. B.	10.9	11.1	....	11.9	11.7	....
G. H.	12.2	10.2	11.5	11.9	11.5	11.7
F. K.	10.9	11.7	11.9	11.5	11.5	....
F. L.	10.9	11.7	....	11.3	11.1	11.3
R. M. (case 5)	11.3	12.2	11.9	12.2	12.2	....
R. M. (case 6)	11.3	11.1	11.3	11.7	11.3	....
E. T.	11.1	11.1	11.9	11.9	11.1	11.6
C. T.	10.2	8.7	8.9	11.1	11.7	11.5
J. V.	11.1	11.1	11.5	11.7	11.7	11.5
P. Y.	11.5	11.7	10.2	11.1	11.7	....
M. Y.	11.7	11.3	10.9	10.7	....	....

TABLE 6.—*The Values for Serum Phosphorus for Premature Infants Receiving Vitamin D Milk*

Patient	Phosphorus per 100 Cc. Serum, Mg.					
	1 mo.	2 mo.	3 mo.	4 mo.	5 mo.	6 mo.
F. B.	7.1	7.0	...	7.9	6.9	...
G. H.	6.2	6.9	7.6	7.6	6.2	6.5
F. K.	7.1	6.9	6.6	7.6	6.2	...
F. L.	6.6	6.6	...	6.0	5.8	6.4
R. M. (case 5)	6.9	7.8	8.4	6.4	6.1	...
R. M. (case 6)	7.0	7.4	7.6	7.1	7.1	...
E. T.	7.4	6.4	7.0	7.4	...	6.9
C. T.	7.7	4.5	5.6	7.5	6.5	6.5
J. V.	7.0	6.3	6.9	6.4	7.6	7.8
P. Y.	7.0	5.9	5.8	6.8	6.3	...
M. Y.	7.4	6.5	7.0	6.9	6.6	...

and the sixth month. Twins (P. Y. and M. Y.) showed clinical signs of rickets also. Moderate frontal bossing from the third to the sixth month and epiphyseal enlargement at the fifth month were noted in one twin (P. Y.). The other twin (M. Y.), in addition to the findings in the former, had a moderate rosary in the third and fourth months. We observed that rachitic manifestations noted at one time were less noticeable or were absent subsequently. This clinical observation coincides with the roentgen observations, which are indicated in table 8 and which will be discussed later.

Chemical Considerations.—Values for serum calcium and inorganic phosphorus are indicated in tables 5 and 6, respectively, and the calcium-phosphorus products in table 7. It will be seen that these values were consistently at high normal levels, except in 1 infant (C. T.), who showed slightly low values for serum

calcium and inorganic phosphorus and therefore a low calcium-phosphorus product in the second (Ca 8.7 × P 4.5 = 39) and third months (Ca 8.9 × P 5.6 = 50). The infant did not show clinical signs of rickets and had doubtful roentgen signs at the second month and a B_1 roentgen sign at the third month. To our knowledge, normal values for serum calcium and phosphorus and a normal calcium-phosphorus product have not been reported for the premature infant. The values for the full term infant must therefore serve as a basis for comparison, and this study corroborates our previous observations [8] that from moderate to severe rickets in the premature infant is not reflected in the values for serum calcium or phosphorus.

TABLE 7.—*The Calcium-Phosphorus Products for Premature Infants Receiving Vitamin D Milk*

Patient	Calcium-Phosphorus Products					
	1 mo.	2 mo.	3 mo.	4 mo.	5 mo.	6 mo.
F. B.	78	77	..	94	81	..
G. H.	76	70	87	90	71	76
F. K.	77	81	79	87	71	..
F. L.	72	77	..	68	64	72
R. M. (case 5)	88	95	100	78	74	..
R. M. (case 6)	79	82	86	83	80	..
E. T.	82	71	83	88	..	80
C. T.	79	39	50	83	76	75
J. V.	78	70	79	75	89	90
P. Y.	81	69	59	75	74	..
M. Y.	87	73	76	74	..	..

TABLE 8.—*The Degree and Stage of Rickets in Premature Infants Receiving Vitamin D Milk*

Patient	Degree and Stage of Rickets*					
	1 mo.	2 mo.	3 mo.	4 mo.	5 mo.	6 mo.
F. B.	E	E	E	B_1	B_1	C_1
G. H.	E	E	E	E	E	E
F. K.	E	B_1	B_1	B_1	B_1	B_1
F. L.	E	E	D	B_1	B_1	B_1
R. M. (case 5)	E	D	E	E	E	E
R. M. (case 6)	E	D	B_1	B_1	B_1	C_1
E. T.	E	E	B_1	B_1	B_1	C_1
C. T.	E	D	B_1	B_2	C_1	C_1
J. V.	E	A_1	A_1	A_1	B_1	B_1
P. Y.	E	E	D	B_1	B_1	C_1
M. Y.	E	D	B_1	B_1	B_1	C_1

Roentgenologic Considerations.—Roentgen observations are indicated in table 8, in which they may be compared with the clinical and chemical findings month by month. They are summarized month by month in table 6 for convenience of comparison.

Dr. Martha M. Eliot of the Children's Bureau, Washington, D. C., gave assistance in the interpretation of the roentgenograms and suggested the use of the letters A, B, C, D and E, to indicate the type of rickets as follows: A, active progressive rickets without evidence of healing; B, the rachitic process in balance, that is, with evidence of healing in the presence of continued activity; C, healed rickets without evidence of activity; D, doubtful rickets, and E, no rickets. The degree of the rachitic involvement is graded by the numbers 1, slight; 2, moderate; 3, marked, and 4, severe.

A study of the serial roentgenograms over the period of observation demonstrated that the infants who received vitamin D milk as the sole source of the antirachitic factor did not in any instance have severe rickets, as compared with those in the control group previously reported on.[8] Of the 11 infants, 2 were free from rickets throughout (G. H. and R. M. [case 5]). R. M. (case 5) showed doubtful signs in the roentgenogram at the second month but thereafter was normal. Of the others, the majority showed a slight rachitic involvement of the B type from the second to the fifth or sixth month, indicating that healing took place in the presence of continued mild activity. By the sixth month the rickets in 6 of the 11 infants was designated as C_1. J. V. had slight active rickets (A_1) at the second, third and fourth months without progression but without evidence of healing until the fifth month. C. T. had moderate rickets (B_2) at the fourth month. He was the only infant who at any time had slightly low values for

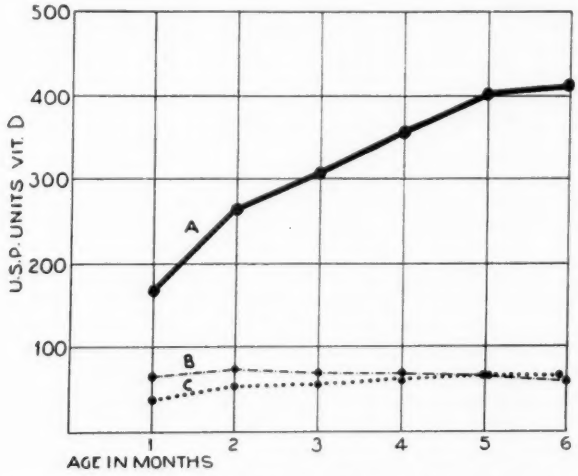

Chart 1.—Comparison of the total daily intake of vitamin D (*A*) with the daily intake of vitamin D per kilogram of weight (*B*) and per centimeter of length (*C*) in premature infants.

serum calcium and inorganic phosphorus, but these occurred during the second and third months, when the roentgenograms showed doubtful and B_1 signs of rickets, respectively. By the fifth month the rickets had entirely healed.

COMMENT

In evaluating any antirachitic factor incorporated in milk it is necessary to take into consideration the daily intake of milk, which in turn is probably influenced by the weight and by the height as well as by the growth rate and by the individual infant's appetite, management and state of health. It will be seen in table 2 and chart 1 that, as with any other form of milk, there was a steady increase in the amount ingested up to the sixth month. Two infants took 1,000 cc. per day by the fourth month, and 5 infants took the same amount by the fifth month. In

comparing this total daily intake of milk with the daily intake of vitamin D per kilogram of body weight at the various months, it is of interest to note that the intake of vitamin D per kilogram remained practically constant throughout the period of observation. Therefore, the mild form of rickets which developed in some of these infants from the second to the fourth months and thereafter healed spontaneously did so with an unvarying level of antirachitic substance as represented by the

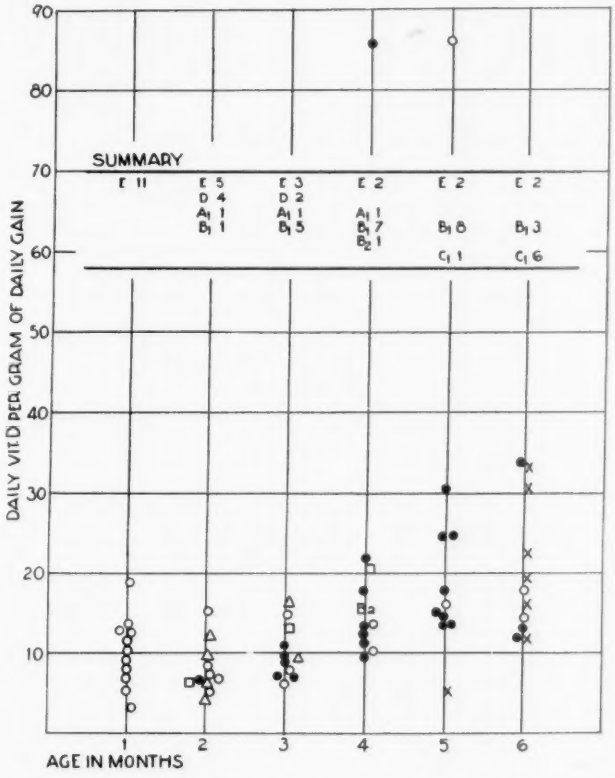

Chart 2.—The relationship of the daily intake of vitamin D per gram of daily gain in weight to the degree and type of rickets in premature infants. In this and chart 3 the circles indicate a normal condition; the triangles, doubtful rickets; the squares, mild active rickets; the solid clots, mild rickets with healing, and the crosses, healed rickets without evidence of activity.

intake per kilogram. While there seemed to be a slight gradual increase in the daily intake per centimeter of length, the month-to-month differences were not significant, and the intake per centimeter remained practically constant throughout, as compared with the total daily intake. A predominating influence of either of these factors on the development or healing of the rachitic process cannot therefore be observed.

The possible relation of the intake of vitamin D to the infants' growth in weight and this to the extent of rickets as shown by the roentgenogram at the various months is suggested in chart 2. It will be seen that slight rachitic activity of the B type, in which healing was present with continued activity, as shown by the roentgenogram, was most commonly seen from the third to the fifth month. Rickets was not observed in the first month, and in only 1 case did B_1 rickets occur in the second month. At the sixth month 2 infants had not shown a sign of rickets throughout the period of observation; 6 infants, who had earlier shown signs of the B_1 type, had healed lesions, and 3 still showed signs of the B_1 type. Moderate rickets (B_2) was observed in

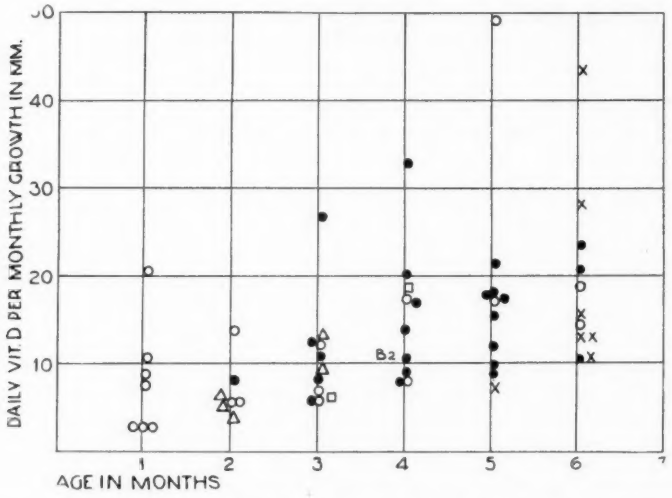

Chart 3.—The relationship of the daily intake of vitamin D per millimeter of monthly growth in length to the degree and type of rickets in premature infants.

1 infant at the fourth month. A summary of these observations is given at the center of the chart. The development of rickets in this group followed closely in time that observed in the control group previously referred to, as well as that observed clinically in any large children's clinic. When rickets did develop, however, it was consistently of mild degree and tended to heal satisfactorily by the sixth month.

The relation of the intake of vitamin D to growth in height and its effect on the development of rickets are shown similarly in chart 3. The findings parallel for the most part those described for growth in weight.

Composite curves of the ratios of the intake of vitamin D to growth in weight and length in charts 2 and 3 are shown in chart 4. For comparison we have also plotted the curves of the average percentage

increase in weight and length for the group month by month. In these curves the low figures at the first month probably reflect the necessary postnatal period of adjustment to food and environment. After the second month there is a gradual decline in the rate of growth in both weight and length.

The curves of the daily intake of vitamin D per unit of growth in weight and length, after an analogous initial period of adjustment, show, on the other hand, a steady rise from the second to the fifth month. It is our opinion that here possibly is the explanation of the fact that the infants showed an early period of approximately two months in which they were free from rickets and that the mild rickets which developed subsequently and healed spontaneously was the result

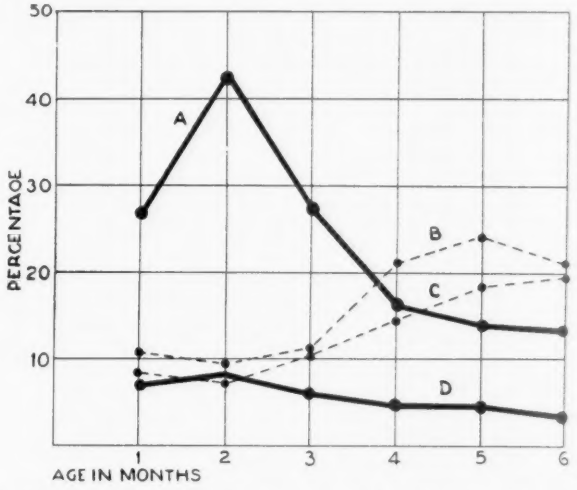

Chart 4.—Composite curves of the ratios of intake of vitamin D to growth in weight (*A*) and length (*D*) compared with the curves of average percentage daily increase in weight (*B*) and monthly increase in length (*C*) in premature infants.

of this latent period during which the intake of vitamin D was low in relation to the impetus for growth. This may be interpreted to mean that we are very near to determining the threshold of the antirachitic requirement for adequate protection and that if to the vitamin D in the milk a supplement is added in the early months, when the need is greatest, one may hope to protect the infant completely from rickets. Such studies are already in progress.

An attempt was made to relate the development and healing of rickets month by month in the individual infant to the variation in the ratio of intake of vitamin D to growth in weight and length. Points on the individual curves in charts 2 and 3 were connected, and the

month-to-month slope was computed. It was thought that a falling slope, equivalent to decreased intake, might mean developing rickets and a rising slope mean healing rickets, as shown by the roentgenogram. Such a relationship, however, was not observed. This would seem to substantiate our opinion that the presence or absence of rachitic manifestations is dependent not so much on the month-to-month level of intake as on the question of whether the intake has been great enough in the early months to prevent subsequent development of the rachitic process during the critical period between the ages of 3 and 5 months.

SUMMARY

Eleven premature infants were given vitamin D milk, from cows fed irradiated yeast, during the first six months of life to determine how far they could be protected from rickets by this means alone.

Clinical evidence of rickets was slight and when present appeared approximately a month later than it was noted in the roentgenogram.

In only one instance was the calcium phosphorus product found to be definitely lowered.

By roentgenogram, two of the infants remained free from rickets throughout the period of study; the other nine showed rickets of mild degree from the third to the fifth month, which had satisfactorily healed by the sixth month without a change in the antirachitic regimen.

Vitamin D milk when used in routine feeding as the sole antirachitic substance has been shown to be inadequate for the complete protection of the premature infant against rickets.

COMPARATIVE DEXTROSE CONTENT OF LUMBAR AND CISTERNAL CEREBROSPINAL FLUID

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The discovery that more than one route may be employed in the removal of cerebrospinal fluid has given rise to the question of whether fluids removed from different loci are alike in their physical and chemical properties. At first, the question concerned itself with the comparative composition of lumbar and ventricular fluids. More recently, the frequent employment of cisternal puncture both in children and in adults has extended the problem to include a comparison of lumbar and cisternal fluid. The problem assumes a practical significance with regard to the dextrose content of the cerebrospinal fluid, which is of diagnostic value in meningitis. Namely, does the determination of the dextrose content in fluid obtained by cisternal puncture furnish information of the same value as the examination of cerebrospinal fluid obtained via the lumbar route?

Some comparative studies of lumbar and cisternal fluid have been reported in the literature. Most of these reports deal with the comparative pressure, cell count, protein test and Wassermann reaction.[1] There are also some data concerning dextrose but the reports by different workers are not consistent. In a study of human subjects, Ayer and Salomon [2] stated: "Sugar is greatest in amount in the ventricular fluid (approximately 0.08 per cent) and least in the lumbar sac (averaging

From the Sarah Morris Hospital for Children and the Department of Chemistry of the Nelson Morris Hospital of the Michael Reese Hospital and from the Cook County Children's Hospital.

1. Weigeldt, W.: Regelmässige Unterschiede in der Zusammensetzung des Liquors an verschiedenen Stellen des Subarachnoidealraumes, München. med. Wchnschr. **68**:838 (July 8) 1921. Baumann, W.: Vergleichende Untersuchungen des bei Zisternenpunktion und Lumbalpunktion entnommenen Liquors, ibid. **74**: 148, 1927. Schenck, H.: Vergleichende Untersuchungen des gleichzeitig entnommenen Zisternen-und Lumballiquors, Ztschr. f. d. ges. Neurol. u. Psychiat. **111**:724, 1927. Schonfeld: Untersuchungen zur Frage der Einheitlichkeit der Rückenmarksflüssigkeit in den verschiedenen Bezirken an Fällen von Dermatosen, Tripper und Frühsyphilis, Arch. f. Dermat. u. Syph. **139**:284, 1922. Kinoshita, S.: Combined Puncture in Syphilis, Jap. J. Dermat. & Urol. **32**:111 (Oct.) 1932, **33**:80 (May) 1932.

2. Ayer, J., and Salomon, H.: Cerebrospinal Fluid from Different Loci, Arch. Neurol. & Psychiat. **14**:303 (Sept.) 1925; in The Human Cerebrospinal Fluid, Association for Research in Nervous and Mental Diseases, New York, Paul B. Hoeber, Inc., 1926.

about 0.06 per cent) with the cisternal fluid showing a value between these two." These authors also studied cerebrospinal fluid from various loci in certain pathologic conditions, but mainly with reference to the cells, organisms and Wassermann reaction.

Fremont-Smith and Ayer,[3] on the other hand, gave the amount of sugar as from 50 to 75 mg. in the lumbar fluid, from 50 to 75 mg. in the cisternal fluid and from 55 to 80 mg. in the ventricular fluid.

In a study of the sugar content of lumbar and cisternal fluid in normal conditions and in cases of neurosyphilis, Reese [4] found the sugar in the cisternal fluid of normal persons to average 65 mg. He gave no detailed figures on the sugar content of the fluid of patients with meningitis but stated that in meningitic conditions—other than syphilitic—the dextrose content of the cisternal fluid is 40 mg. and of the lumbar fluid from 10 to 20 mg.

We have made a more thorough study than the authors cited of the comparative dextrose contents of lumbar and cisternal fluid, primarily from the point of view of the diagnostic value in cases of meningitis. At the beginning of our study we attempted to compare a series of results on cerebrospinal fluid obtained by cistern puncture with a previous series on lumbar fluid; we found, however, that unless the lumbar and cisternal fluids were obtained simultaneously from the same patient, the comparisons were of no scientific value. We therefore used only the results obtained when combined punctures were made.

We want to make clear at the outset that we do not advocate the routine use of combined lumbar and cisternal punctures or of cisternal puncture alone. We decidedly prefer lumbar to cisternal puncture for diagnosis, and also for treatment when sufficient drainage can be obtained by the lumbar route. During the time that the combined punctures reported in this paper were made, most of our patients with meningitis were treated by lumbar puncture alone. Nevertheless, there are indications for cisternal puncture and for combined puncture in persons with certain types and at certain stages of meningitis. In some of our patients, for instance, cisternal punctures had to be resorted to when drainage was desired for therapeutic purposes and only a few cubic centimeters of fluid could be withdrawn by the lumbar route. This happened especially in cases of purulent meningitis when the fluid became thick. In some cases of meningococcic meningitis we were able to obtain fluid by lumbar puncture but not in large enough amounts to permit the introduction of serum intraspinally without fear of increasing intraspinal pressure. In such cases we had to follow the lumbar puncture immediately by a cisternal puncture. We had patients also in whom

3. Fremont-Smith, F., and Ayer, J.: Cerebrospinal Fluid in Differential Diagnosis, J. A. M. A. **88**:1078 (April 2) 1927.

4. Reese, H. H.: Cerebro-spinal Fluid: Comparative Studies After Cisternal and Lumbar Puncture, Wisconsin M. J. **26**:506, 1927.

the spinal fluid pressure was so high that we deemed it advisable to make a combined cisternal and lumbar puncture in order to facilitate drainage.

In instances in which the clinical circumstances called for combined puncture, we had the opportunity of studying cerebrospinal fluid obtained simultaneously by the lumbar and cisternal routes in the same patients.

Occasionally a combined puncture was made when the clinical picture was suggestive of meningitis, particularly of the tuberculous type, but the condition was subsequently shown to be nonmeningitic. We have used the results obtained on fluids from these patients as a base line for our comparisons with values for meningitic patients. They are in a sense our "normal controls." Although we realize that none of these children were healthy, we feel that their use in this manner introduces no error of appreciable magnitude into our work, especially since we confirmed our findings by a series of experiments on normal dogs. However, as pointed out elsewhere,[5] we prefer to use the classification "nonmeningitic" rather than "normal" because lumbar and cisternal punctures were made only when existing symptoms of disease gave clinical indication for the procedure.

METHODS

For the determination of dextrose we employed the Somogyi modification of the Shaffer-Hartmann method.[6] In this method the nondextrose reducing substances are removed with the protein precipitant, and the results are therefore lower than those given by most of the usual methods. The method is preferable to those ordinarily used because it gives "true dextrose" values.

The fluid was obtained during fasting. Care was also taken that the patient received no injections of dextrose parenterally or drugs affecting the dextrose content of the blood.

The fluids were kept cold and brought to the laboratory immediately after withdrawal. Under these conditions we found by numerous experiments that there was no appreciable glycolysis.

CLASSIFICATION

We classified our patients into two main groups: (*a*) those who suffered from diseases other than meningitis and (*b*) those who suffered from some form of meningitis.

From our series of nineteen nonmeningitic patients we obtained twenty-three specimens of lumbar fluid and the same number of specimens of cisternal fluid by combined lumbar and cisternal puncture.

From thirty-eight meningitic patients we obtained forty-nine specimens of each fluid. This series included fluids from patients with tuberculous meningitis, meningococcic meningitis before and after serum treatment, and meningitis due to the streptococcus, the pneumococcus and the influenza bacillus.

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5. Levinson, A.: Cerebrospinal Fluid in Health and Disease, St. Louis, C. V. Mosby Company, 1929.

6. Somogyi, M.: Sugar Determination, J. Biol. Chem. **70**:599 (Nov.) 1926: Reducing Non-Sugar and True Sugar in Human Blood, ibid. **75**:33 (Oct.) 1927.

RESULTS

NONMENINGITIC PATIENTS.—Our series of nineteen nonmeningitic patients was further subdivided into two categories. Eight were proved by the clinical course to have had no lesions of the central nervous system (table 1, fig. 1). The dextrose

TABLE 1.—*Comparative Dextrose Content of the Lumbar and the Cisternal Cerebrospinal Fluid in Nonmeningitic Patients (Without Pathologic Changes in the Central Nervous System)* *

	Diagnosis	Dextrose Content (Mg. per 100 Cc.) Lumbar	Cisternal	Difference
1	Pulmonary tuberculosis	49	49	0
		67†	71	+ 4
2	Pharyngitis, otitis	69	70	+ 1
3	Whooping cough	48	47	— 1
4	Pulmonary tuberculosis	53	55	+ 2
		40†	44	+ 4
5	Typhoid	58	55	— 3
6	Subpectoral abscess	62	67	+ 5
7	Dysentery	76	81	+ 5
8	Dysentery	48	59	+11
	Average	57	60	± 3.6

* In this and succeeding tables the plus sign signifies the higher values for dextrose in the cisternal fluid and the minus sign the lower values.

† In tables 1, 2, 5 and 6 the dagger indicates determinations made on the same patient on different days.

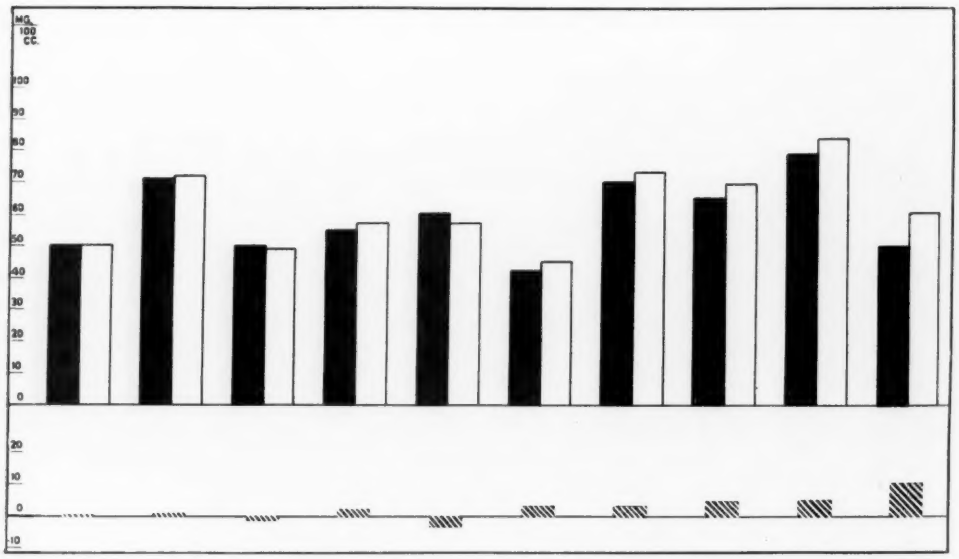

Fig. 1.—Chart showing the comparative dextrose content of the lumbar and the cisternal cerebrospinal fluid of nonmeningitic patients without pathologic changes in the central nervous system. In human subjects without pathologic changes in the central nervous system, just as in normal dogs, the dextrose content of the cisternal fluid is equal to that of the lumbar fluid or is only a few milligrams higher. In figures 1, 2, 3, 5, 6, 7 and 8 the solid black columns indicate the lumbar fluid and the white columns the cisternal fluid. The shaded columns indicate the difference (the excess of cisternal fluid is shown above the line and the excess of lumbar fluid below the line).

content of the lumbar fluid of these patients ranged from 40 to 76 mg. per hundred cubic centimeters and averaged 57 mg. These values are within the "normal" limits as established by our earlier work, in which we found the normal range to be from 38 to 75 mg. per hundred cubic centimeters.[7]

TABLE 2.—*Comparative Dextrose Content of the Lumbar and the Cisternal Cerebrospinal Fluid of Nonmeningitic Patients (With Pathologic Changes of the Central Nervous System)*

	Diagnosis	Dextrose Content (Mg. per 100 Cc.) Lumbar	Cisternal	Difference
1	Postencephalitis	60	60	0
2	Encephalitis	62	62	0
3	Spastic paraplegia	53	52	— 1
4	Meningism	82	80	— 2
5	Little's disease	96	94	— 2
6	Idiocy	51	54	+ 3
7	Epilepsy	53	46	— 7
8	Amaurotic family idiocy	90	99	+ 9
9	Epilepsy	78	91	+13
10	Acute anterior poliomyelitis	52	67	+15
11	Cerebellar tumor	69	62	— 7
		63†	76	+13
		63†	41	—22
	Average	67	68	± 7.2

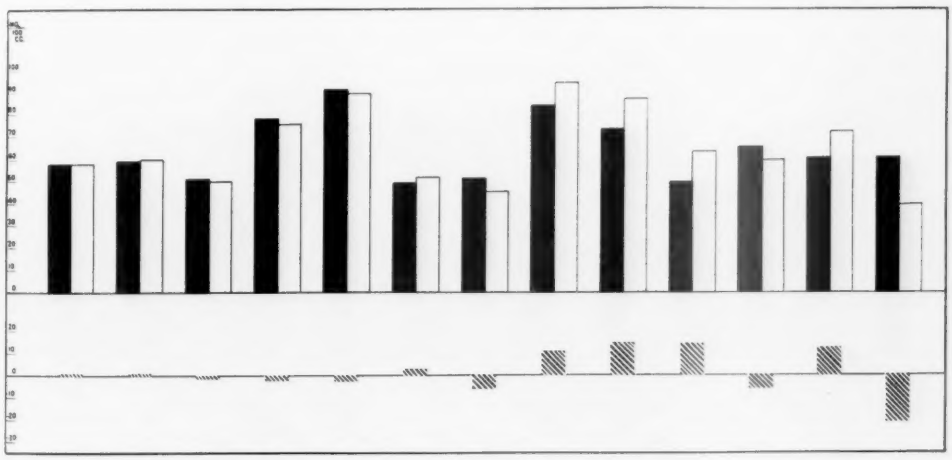

Fig. 2.—Chart showing the comparative dextrose content of the lumbar and the cisternal cerebrospinal fluid of nonmeningitic patients with some pathologic changes in the central nervous system. In nonmeningitic patients with disturbances of the central nervous system, the dextrose content of the cerebrospinal fluid often is raised but that of the lumbar and cisternal fluid is approximately equal.

The cisternal fluid of these patients (drawn simultaneously with the lumbar fluid) had a dextrose content of from 44 to 81 mg. In one instance the cisternal fluid was 11 mg. higher in dextrose content than the lumbar; in all the others

7. Cohn, D. J.; Levinson, A., and McCarthy, F.: Physiological Variations in the Glucose Ratio of Blood and Cerebrospinal Fluid, Am. J. Physiol. **103**:613, 1933.

the difference was 5 mg. or less. From these results it would appear that cisternal fluid normally is either about equal in content to the lumbar fluid or a few milligrams higher.

The remaining eleven patients in this series all showed some pathologic change in the central nervous system but not meningitis (table 2, fig. 2). The average of thirteen determinations of the dextrose content of the lumbar fluid was

TABLE 3.—*Comparative Dextrose Content of the Lumbar and the Cisternal Cerebrospinal Fluid of Normal Dogs (Pentobarbital Sodium Anesthesia)*

	Dextrose Content (Mg. per 100 Cc.)		
	Lumbar	Cisternal	Difference
1	62	62	0
2	58	59	+ 1
3	64	66	+ 2
4	69	71	+ 2
5	52	56	+ 4
6	79	75	− 4
7	78	84	+ 6
8	53	60	+ 7
9	54	63	+ 9
10	69	79	+10
Average	64	68	± 5

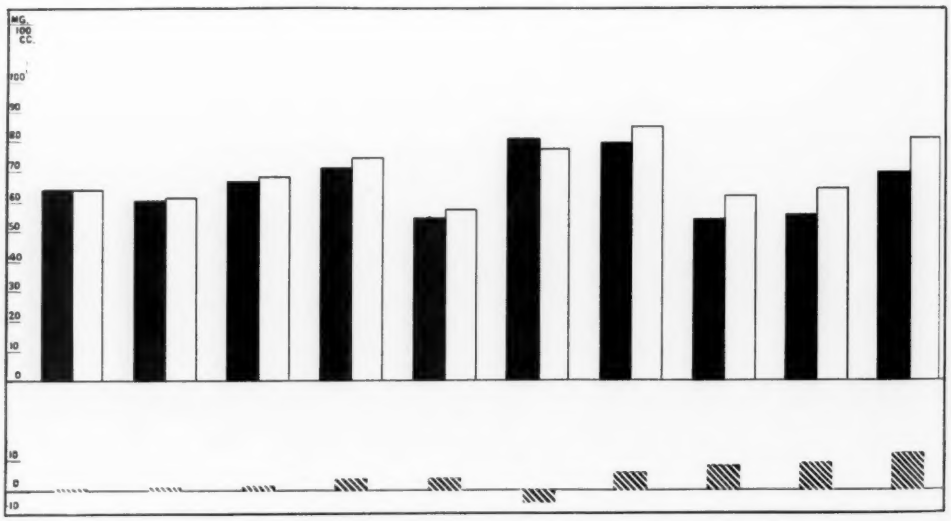

Fig. 3.—Chart showing the comparative dextrose content of the lumbar and cisternal cerebrospinal fluid of normal dogs under pentobarbital sodium anesthesia. Under basal conditions, as in the case of fasting normal dogs, cerebrospinal fluid obtained by lumbar and cisternal puncture has approximately the same dextrose content, but the dextrose content of the cisternal fluid is usually a few milligrams higher than that of the lumbar fluid.

67 mg, and that for the cisternal fluid, 68 mg. The deviations of individual patients in this series from the normal with respect to the dextrose content of both the cisternal and the lumbar fluid was larger than in the first group; the differences

between the dextrose content of the lumbar and that of the cisternal fluid drawn simultaneously averaged 7.2 mg.

Normal Dogs.—To confirm our results in human beings we did a series of combined punctures in normal dogs. We used pentobarbital sodium as an anesthetic because its effect on the dextrose content of the blood was found to be slight. In none of the ten dogs on whom spinal puncture was made was there any greater difference than 10 mg. between the dextrose content of the cisternal and that of the lumbar fluid. In six of them it was 4 mg. or less (table 3, fig. 3). This indicates that under normal conditions in dogs the dextrose content of the cisternal fluid is either equal to that of the lumbar fluid or a few milligrams higher, thus coinciding with the results found in human beings.

We went one step further and determined the dextrose content of the cisternal and lumbar fluids in dogs over a period of several hours at thirty minute intervals (fig. 4). The spinal and cisternal needles were left in situ with the stylets in place, and these were removed from both needles simultaneously

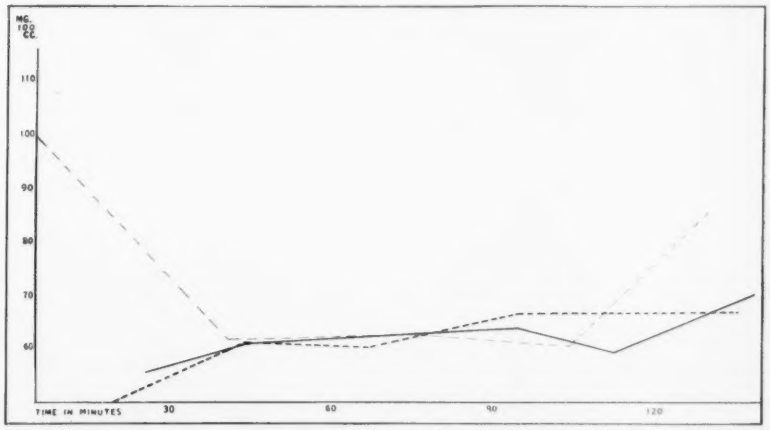

Fig. 4.—Dextrose levels in the blood and the cerebrospinal fluid of the normal dog. Changes in the dextrose content of the blood are reflected, but with a definite time lag, in both the lumbar and the cisternal cerebrospinal fluid. The variations in the fluids drawn at intervals over a period of several hours are less marked than in blood. The fine broken line indicates the blood; the heavy broken lines, the lumbar fluid, and the unbroken line, the cisternal fluid.

for the collection of the specimens. It will be seen from the curve in figure 4 that in this experiment the dextrose content of the cisternal and that of the lumbar fluid were at approximately the same level throughout.

The experiments on normal dogs confirmed our observation on "nonmeningitic" human patients and justified our use of the latter as "normal" controls for comparison with meningitic patients.

Meningitic Patients.—It is well known that the dextrose content of the lumbar fluid is considerably decreased in all forms of meningitis, but apparently the relationship of the dextrose content of the cisternal fluid to that of the lumbar fluid in meningitis is not well known, as values for the cisternal fluid are often used for diagnostic purposes.

Tuberculous Meningitis: In our series of eighteen patients with tuberculous meningitis (table 4, fig. 5), the dextrose content in the lumbar fluid ranged from 0 to 33 mg. per hundred cubic centimeters, with an average of 12 mg. This is very much below the normal value for the lumbar fluid. On the other hand,

TABLE 4.—*Comparative Dextrose Content of the Lumbar and the Cisternal Cerebrospinal Fluid of Persons with Tuberculous Meningitis*

	Dextrose Content (Mg. per 100 Cc.)		
	Lumbar	Cisternal	Difference
1	18	24	+ 6
2	8	20	+12
3	5	18	+13
4	12	25	+13
5	0	16	+16
6	16	33	+17
7	2	23	+21
8	19	43	+24
9	0	26	+26
10	5	31	+26
11	19	46	+27
12	25	52	+27
13	10	38	+28
14	24	53	+29
15	33	63	+30
16	11	47	+36
17	8	53	+45
18	0	68	+68
Average	12	38	+26

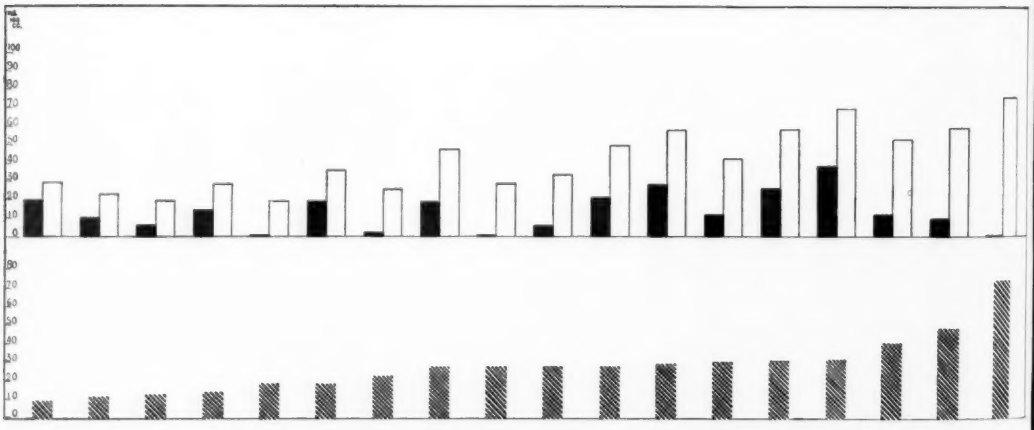

Fig. 5.—The comparative dextrose content of the lumbar and the cisternal cerebrospinal fluid of persons with tuberculous meningitis. In tuberculous meningitis there is a marked reduction of dextrose in the fluid obtained by lumbar puncture. The dextrose in the fluid obtained by cisternal puncture is often reduced but never as much as in the lumbar fluid. At times the dextrose content of the cisternal fluid is within the normal limits even when the dextrose content of the lumbar fluid is very much below normal.

the dextrose content of the cisternal fluid, though often reduced, was nevertheless without exception higher than the dextrose content of fluid obtained at the same time from the lumbar region. The dextrose content of the cisternal fluid ranged from 16 to 68 mg. and averaged 26 mg. more than the corresponding figures

for lumbar fluid. In several instances the dextrose content of the cisternal fluid was well within the normal limits, even when the dextrose of the lumbar fluid was very low. In fact, in one case in which dextrose was absent from the lumbar fluid the amount in the cisternal fluid was 68 mg. per hundred cubic centimeters.

We were able to study the dextrose levels of lumbar and cisternal fluid on several successive days of illness in one patient with tuberculous meningitis. It will be noted that the dextrose content of the lumbar fluid decreased continuously, whereas that of the cisternal fluid remained almost stationary at a higher level, thus bringing about a continuously increasing difference between the dextrose content of the lumbar and that of the cisternal fluid (fig. 6).

Meningococcic Meningitis: Five patients with meningococcic meningitis from whom specimens of lumbar and cisternal fluid were obtained before they were treated with serum showed results similar to those obtained for the patients with tuberculous meningitis. The dextrose content of the lumbar fluid ranged

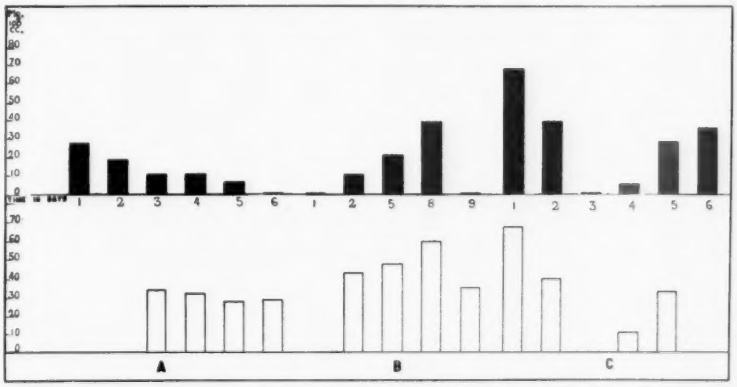

Fig. 6.—Progressive values for dextrose in the lumbar and the cisternal fluid of persons with meningitis. In two patients with tuberculous meningitis the lumbar and the cisternal fluid of whom were examined over a period of several days, the cisternal fluid was found not only to contain more dextrose than the lumbar fluid but to remain almost stationary at a higher level. On the other hand, in the patient with streptococcic meningitis the dextrose content of both fluids remained approximately equal throughout. *A* and *B* indicate the patients with tuberculous meningitis and *C* the one with streptococcic meningitis.

between 0 and 23 mg. per hundred cubic centimeters, with an average of 9 mg. The dextrose content of the cisternal fluid remained much higher, ranging from 11 to 44 mg. and averaging 30 mg. (table 5, fig. 7).

In the same table are shown a series of determinations on patients suffering from meningococcic meningitis who had been treated with serum. The dextrose content of the lumbar fluid averaged 34 mg. per hundred cubic centimeters, which is much nearer to the normal than the average value for the untreated patients. The values for the cisternal fluid averaged 42 mg. and the differences between simultaneously drawn lumbar and cisternal fluid approached those for nonmeningitic patients.

Purulent Nonmeningococcic Meningitis: In a limited series of patients with meningitis due to the influenza bacillus, the pneumococcus and the streptococcus,

TABLE 5.—*Comparative Dextrose Content of the Lumbar and the Cisternal Cerebrospinal Fluid of Persons with Meningococcic Meningitis*

	Dextrose Content (Mg. per 100 Cc.)		
	Lumbar	Cisternal	Difference
Before Serum			
1	0	11	+11
	0†	27	+27
2	15	29	+14
3	0	20	+20
4	23	47	+24
5	15	44	+29
Average	9	30	+21
After Serum			
6	58	58	0
7	58	55	— 3
8	13	18	+ 5
	21†	26	+ 5
	26†	42	+16
	23†	45	+22
9	39	44	+ 5
10	34	49	+15
Average	34	42	± 9

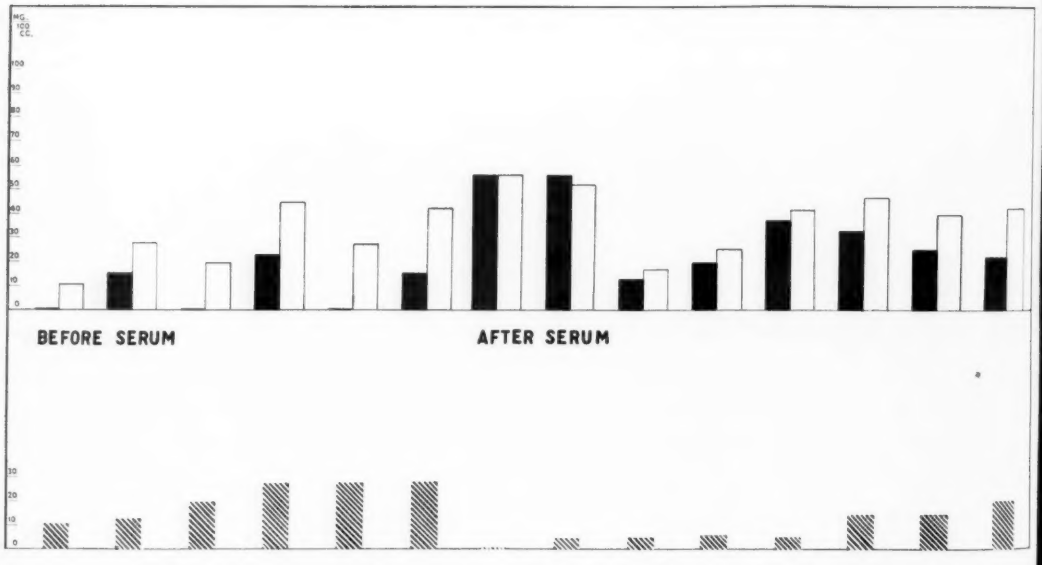

Fig. 7.—Comparative dextrose content of the lumbar and the cisternal cerebrospinal fluid of persons with meningococcic meningitis. Before the administration of serum the decrease in dextrose content is much more definite and regular in the lumbar than in the cisternal fluid. After the administration of serum the dextrose levels in both the lumbar and the cisternal fluid tend to approach the normal values.

we found the dextrose content of the lumbar fluid to be universally low. Dextrose was absent in ten of the eleven instances. In all but one of the cases of pneumococcic and streptococcic meningitis, dextrose was absent or present in very small amount in the cisternal as well as in the lumbar fluid (table 6, fig. 8). In cases

TABLE 6.—*Comparative Dextrose Content of the Lumbar and the Cisternal Cerebrospinal Fluid of Persons with Purulent Nonmeningococcic Meningitis*

	Dextrose Content (Mg. per 100 Cc.)		
	Lumbar	Cisternal	Difference
Streptococcic Meningitis			
1	0	0	0
2	0	0	0
3	0	0	0
4	0	8	+ 8
5	0	38	+38
Average	0	9	+ 9
Pneumococcic Meningitis			
1	0	0	0
2	8	8	0
Average	4	4	0
Due to the Meningitis Influenza Bacillus			
1	0	13	+13
2	0	14	+14
	0†	15	+15
3	0	24	+24
Average	0	16	+16

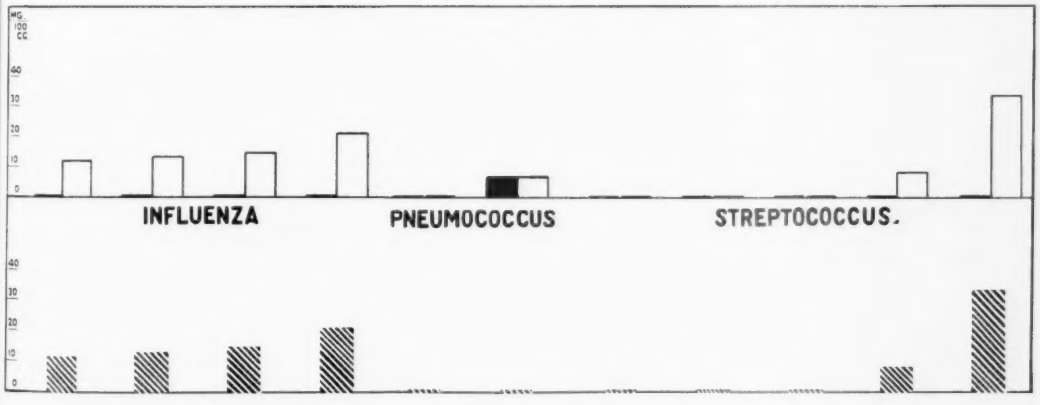

Fig. 8.—Comparative dextrose content of the lumbar and the cisternal cerebrospinal fluid of persons with purulent nonmeningococcic meningitis. The values for dextrose in patients with meningitis due to the influenza bacillus were found to be similar to those for patients with tuberculous meningitis; namely, the dextrose content of the cisternal fluid, while low, nevertheless was higher than that of the lumbar fluid. In contrast to this, in patients with pneumococcic and in those with streptococcic meningitis, dextrose was absent from the cisternal as well as from the lumbar fluid in all but one instance.

of meningitis due to the influenza bacillus the dextrose content of the cisternal fluid, although low, was not as low as that in cases of streptococcic and pneumococcic meningitis and more closely resembled the content of fluid from patients with tuberculous meningitis.

COMMENT

In the series of nonmeningitic patients studied, as well as in normal dogs, the dextrose content was found to be about the same in simultaneously obtained lumbar and cisternal fluid or only a few milligrams higher in the cisternal fluid. From these results, as well as from results previously reported of the comparison of dextrose values for blood and cerebrospinal fluid, it appears probable that there is an equilibrium between the dextrose content of the blood and that of the ventricular, cisternal and lumbar fluids, so that they have approximately equal dextrose concentrations under normal basal conditions. When the dextrose concentration of the blood is increased for any reason, the dextrose content in the cisternal fluid rises before that in the lumbar fluid owing to the fact that the cistern is closer to the ventricles and choroid plexus—the point of origin of the cerebrospinal fluid. During periods of recession of the dextrose level of the blood, the dextrose content of the lumbar fluid may remain higher than that of the cisternal fluid, but such instances are rare.

In meningitis, the equilibrium between the cisternal and the lumbar fluid is disturbed, and the lumbar fluid is often found to contain considerably less dextrose than the cisternal fluid. This may be due either to interference in the circulation of the cerebrospinal fluid, which lowers the rate of diffusion of the dextrose from the cisternal to the lumbar fluid, or to the more rapid disappearance of dextrose from the lumbar than from the cisternal fluid.

We are not as yet prepared to say whether the low values for dextrose found in the cisternal as well as in the lumbar fluid of the majority of our patients with purulent nonmeningococcic meningitis are of value in differentiating these types of meningitis from the tuberculous and meningococcic forms, in which the dextrose content of the cisternal fluid was consistently higher than that of the lumbar fluid. The low values may have been due to the advanced stage and severity of the disease in our small series.

Is it possible to utilize determinations of dextrose in the cisternal fluid for the diagnosis of meningitis? Our studies show that a diagnosis should not be made on the basis of the dextrose content of cisternal fluid alone, as the dextrose content of the cisternal fluid may be normal or only slightly decreased at the same time that the lumbar fluid is greatly decreased. In such instances the diagnosis of meningitis would be missed if the values for dextrose in the cisternal fluid alone were relied on. We believe that a marked fall in the dextrose content of the cisternal as well as of the lumbar fluid in the same patient indicates a very poor prognosis. However, considering the untoward possibilities in cisternal puncture, the advisability of a combined puncture for prognostic

reasons is questionable. We therefore believe that cisternal puncture, alone or combined with lumbar puncture, is best indicated in the treatment of meningitis and not in establishing a diagnosis or prognosis.

SUMMARY

A study has been made of the comparative dextrose content of the lumbar and the cisternal cerebrospinal fluid obtained from nonmeningitic and meningitic patients and from normal dogs.

In nonmeningitic patients the dextrose content of the cisternal fluid was found to be either equal to that of the lumbar fluid or slightly higher. The dextrose content of the lumbar fluid of those patients in whom no pathologic change in the nervous system was found averaged 57 mg. per hundred cubic centimeters, and that of the cisternal fluid, 60 mg. The results on normal dogs were similar to those on human beings.

In patients with tuberculous meningitis and in untreated patients with meningococcic meningitis, the dextrose content of the lumbar fluid was always reduced. The dextrose content of the cisternal fluid, while usually lower than normal, was not as low as that of the lumbar fluid. In some instances the dextrose content of the cisternal fluid was within the normal range, even though dextrose was absent or very little was present in the lumbar fluid. In patients with meningococcic meningitis after serum treatment the values for dextrose in the cisternal and lumbar fluid were much closer to the normal than the values found for untreated patients, and the differences between the levels in the two fluids were smaller.

In the majority of a limited series of fluids from patients with nonmeningococcic purulent meningitis, particularly of the pneumococcic and streptococcic types, there was a very low amount of dextrose or none in the cisternal as well as in the lumbar fluid.

Determinations of the dextrose content of the lumbar fluid are more reliable for the diagnosis of meningitis than determinations made on the cisternal fluid because the dextrose content of the cisternal fluid is seldom reduced as greatly as that of the lumbar fluid.

CREATINURIA OF INFANCY AND CHILDHOOD

I. NORMAL VARIATIONS: CREATINE TOLERANCE TESTS AND THE EFFECT OF AMINO-ACETIC ACID IN NORMAL INFANTS

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AND

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The metabolism of creatine and creatinine has attracted widespread interest in recent years. Although creatinine was first recognized in 1832,[1] the impetus to study its metabolism arose from the publication by Folin [2] in 1904 of a simple method for its determination. Numerous investigations during the last three decades have established the constancy of the presence of creatinine in the urine and of creatine under certain normal and pathologic conditions. The regularity of the excretion of creatinine indicated that it was a waste product of the body, but the function of creatine remained an open question, although the Eggletons [3] and Fiske and Subbarow [4] have recently demonstrated the importance of phosphocreatine in muscle metabolism.

The classic monograph by Hunter [5] summarized the results of studies of creatine and creatinine up to 1928. This was supplemented by the review of Rose [6] in 1933. No attempt, therefore, will be made here to

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1. Chevreul, M. E.: Recherches sur la composition chimique du bouillon de viande (extrait d'un rapport sur le bouillon de la compagnie hollandaise fait à l'Academie des Sciences par M. Chevreul le 19 mars 1832), J. Pharm. **21**:231, 1835; J. prakt. Chem. **6**:120, 1835.

2. Folin, O.: Beitrag zur Chemie des Kreatinins und Kreatins im Harne, Ztschr. f. physiol. Chem. **41**:223, 1904; Approximately Complete Analyses of Thirty "Normal" Urines, Am. J. Physiol. **13**:45, 1905.

3. Eggleton, P., and Eggleton, G. P.: The Inorganic Phosphate and a Labile Form of Organic Phosphate in the Gastrocnemius of the Frog, Biochem. J. **21**:190, 1927; The Physical Significance of "Phosphagen," J. Physiol. **63**:155, 1927; Further Observations on Phosphagen, ibid. **65**:15, 1928; A Method of Estimating Phosphagen and Some Other Phosphorus Compounds in Muscle Tissue, ibid. **68**:193, 1929.

4. Fiske, C. H., and Subbarow, Y.: The Nature of the "Inorganic Phosphate" in Voluntary Muscle, Science **65**:401, 1927; The Isolation and Function of Phosphocreatine, ibid. **67**:169, 1928; Phosphocreatine, J. Biol. Chem. **81**:629, 1929.

5. Hunter, Andrew: Creatine and Creatinine, New York, Longmans, Green & Co., 1928.

6. Rose, W. C.: The Metabolism of Creatine and Creatinine, in Annual Review of Biochemistry, Stanford University, Calif., Stanford University Press, 1933, vol. 2, p. 187.

cover the literature except as it pertains to the specific problems studied. The investigations deal with the creatinuria of infancy, and an attempt is made to correlate and amplify the earlier work on the subject preparatory to a study of the influence of endocrine products on the physiologic creatinuria of infants.

METHODS AND MATERIAL

Normal infants from 3 weeks to 7 months of age were studied. They received formulas of dried whole milk (Klim) with cane sugar, adequately supplemented with orange juice and cod liver oil. The nitrogen content of the Klim and of cereal, when used, was determined by the Kjeldahl method, thus permitting an accurate estimation of the amount of nitrogen ingested.

For the collection of urine the infants were placed on the special bed devised by Hoag [7] for use in studies of metabolism, which afforded accurate records of the time of voiding at the beginning and end of each period. Twenty-four hourly periods were begun at or near 10 a. m. The urine was preserved with toluene, and analyses were always started shortly after the completion of the period.[8]

All analyses were made in triplicate. The total nitrogen content was determined by the macro-Kjeldahl method, and the creatine and creatinine contents by Folin's method.[9] Creatine was converted into creatinine by boiling with normal hydrochloric acid. Analyses of pure solutions of creatine as well as of creatine added to urine gave from 98 to 100 per cent recovery by this method. In the tables creatine is reported in terms of creatinine. The data in tables 1, 2, 5 and 7 represent the calculated values for exactly twenty-four hours.

In order to compare the data obtained for different infants, creatinine and creatine coefficients were calculated. These represent milligrams of nitrogen excreted as creatinine and creatine, respectively, per kilogram of body weight in twenty-four hours. The total creatine coefficient is the sum of the creatine and creatinine coefficients.

NORMAL VARIATIONS IN THE EXCRETION OF CREATININE AND CREATINE

Creatinine is apparently always excreted in the urine by human beings. Folin [10] was the first to show that the excretion of creatinine by an adult is extremely constant from day to day while he is on a meat-free regimen. The general validity of this conclusion has been repeatedly confirmed, but the constancy has been shown to be relative rather than absolute. In a series of daily determinations on a single subject variations amounting to 10 per cent of the average are not

7. Hoag, L. A.: Apparatus for the Quantitative Collection of Urine and of Stools in Male Infants, Am. J. Dis. Child. **44**:770 (Oct.) 1932.

8. The infants were attended by nurses experienced in metabolic technic.

9. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry, Baltimore, Williams & Wilkins Company, 1932, vol. 2, pp. 518 and 602.

10. Folin, O.: Laws Governing the Chemical Composition of Urine, Am. J. Physiol. **13**:66, 1905.

uncommon,[5] and Schulz [11] has reported a difference between maximum and minimum values of 23.7 per cent in an eleven day experiment.

This constancy of creatininuria is even less striking in infants and children than in adults. The coefficients reported for preformed creatinine in the urine of infants and children have varied from 3.5 to 6.4.[5] Compared with the figures for adults (7.5 to 10 for men and 5 to 8 for women [12]), these coefficients are distinctly low. If, however, the creatine is added to the creatinine and the total creatine coefficient

TABLE 1.—*Excretion of Creatinine and Creatine by Normal Infants*

	Rougichitch*	Rougichitch†	Rougichitch‡	Daniels and Hejinian§	Present Investigation#
Number of cases	28	19	6	9	5
Number of analyses	56	36	12	55	35
Age of infants, months	1½ to 13	1 to 22	5 to 12	2 to 8	1½ to 7
Length of period studied, hours	48	24	24	72	24
Creatinine nitrogen, Mg. per Kg. in 24 hours					
Average	4.63	4.80	4.45	4.28	4.93
Maximum	5.60	5.90	5.10	5.30	5.60
Minimum	3.50	3.80	3.90	3.70	3.70
Coefficient of variability, percentage	10.11	19.63	7.83	7.96	10.96
Creatine nitrogen, Mg. per Kg. in 24 hours					
Average			5.68		3.89
Maximum			7.40		5.10
Minimum			2.30		2.00
Coefficient of variability, percentage			24.68		17.15
Total creatinine plus creatine nitrogen, mg. per Kg. in 24 hours					
Average			10.04		8.86
Maximum			12.20		10.50
Minimum			6.40		7.20
Coefficient of variability, percentage			16.49		10.37

* Rougichitch, O. S.: The Creatinine Coefficient in the Infant, Arch. Dis. Childhood **1**: 348, 1926.

† Rougichitch, O. S.: Uric Acid and Creatinine in the Urine of Infants, Am. J. Dis. Child. **31**: 504 (April) 1926.

‡ Rougichitch, O. S.: The Day and Night Creatinine and Creatine in the Urine of Infants, Arch. Dis. Childhood **1**: 289, 1926.

§ Daniels, A. L., and Hejinian, L. M.: Growth of Infants from the Standpoint of Physical Measurements and Nitrogen Metabolism: I. Creatinine, Am. J. Dis. Child. **37**: 1128 (June) 1929.

Complete data are given in table 2. This summary does not include data for infants W. W., M. M., and R. S.

is calculated, the figures for infants and children range from 4.7 to 11.6 and for the most part fall within the range established for preformed creatinine in normal adults. This congruence of results has led Harding and Gaebler [13] to conclude that the total creatine coefficient (creatine

11. Schulz, W.: Der Verlauf der Kreatininausscheidung im Harn des Menschen mit besonderer Berücksichtigung des Einflusses der Muskelarbeit, Arch. f. d. ges. Physiol. **186**:126, 1921.

12. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry, Baltimore, Williams & Wilkins Company, 1932, vol. 1, p. 458.

13. Harding, V. J., and Gaebler, O. H.: On the Constancy of the Creatine-Creatinine Excretion in Children on a High Protein Diet, J. Biol. Chem. **54**:579, 1922.

plus creatinine nitrogen) is entirely independent of age when the diet, especially the protein intake, is adequate.

Data illustrating the variations in the output of creatine and of creatinine as reported in several investigations of infants are summarized in table 1. This summary does not include all the published work on infants but presents only those investigations in which a relatively large number of subjects were studied. The similarity of the results from the different sources is striking. The data for fifty-one twenty-four hour specimens from eight infants studied in this investigation are presented in detail in table 2. In constructing table 1 the data for the youngest infants (W. W., M. M., and R. S.) were omitted for reasons to be discussed in a subsequent section. With the exception of the three cases mentioned the creatinine coefficients ranged from 3.7 to 5.6 with an average of 4.93. The creatine coefficients ranged from 2 to 5.1 with an average of 3.89. Summation of these two groups of figures gave a range of from 7.2 to 10.5 with an average value of 8.86 for the total creatine coefficient. The variability in the output of creatine by individual infants and by the same infant on different days notably exceeded that for creatinine.

Diurnal fluctuations in the rate of excretion of creatine have been studied. Shaffer[14] has shown that the output of creatinine by a normal man has a remarkably constant rate irrespective of time. The excretion of creatine is far less regular. Denis[15] observed considerable variations in the rate of excretion of creatine by adults suffering from exophthalmic goiter. He was of the opinion that these fluctuations were related to the ingestion of food, the maximum excretion of creatine always occurring after the main meal of the day. Denis and Kramer[16] also related the periodic variations in children to hours of feeding. Powis and Raper,[17] studying normal boys of 2½ and 3 years, found that the rate of excretion of creatine was highest during the morning, less during the later part of the day and very small at night. They attributed this variation in rate of excretion to increased utilization (or destruction) of creatine accompanying the anabolic process of rest. Rougichitch[18] analyzed the urine every three hours for a series of six infants.

14. Shaffer, P.: The Excretion of Kreatinin and Kreatin in Health and Disease, Am. J. Physiol. **23**:1, 1908.

15. Denis, W.: A Note on the Diurnal Variations in Creatine Excretion, J. Biol. Chem. **29**:447, 1917.

16. Denis, W., and Kramer, J. G.: The Influence of Protein Intake on Creatine Excretion in Children, J. Biol. Chem. **30**:189, 1917.

17. Powis, F., and Raper, H. S.: Creatinuria in Children, Biochem. J. **10**:363, 1916.

18. Rougichitch, O. S.: The Day-and-Night Creatinine and Creatine in the Urine of Infants, Arch. Dis. Childhood **1**:289, 1926.

TABLE 2.—*Daily Excretion of Nitrogen, Creatine and Creatinine by Normal Infants*

Patient	Age	Weight, Kg.	Date	Nitrogen Intake, Gm.	Total Urinary Nitrogen, Gm.	Creatinine, Mg.	Creatine as Creatinine, Mg.	Coefficient			Total Creatinine Excreted as Creatine, Percentage
								Creatinine	Creatine	Total	
F. L.	7 mo.	6.32	10/ 4–10/ 5	4.89	3.2801	84.65	55.90	4.97	3.28	8.25	39.8
		6.41	10/ 5–10/ 6	4.89	3.5009	90.76	64.10	5.23	3.71	8.94	41.5
		6.41	10/ 6–10/ 7	4.89	3.6650	96.78	65.14	5.61	3.77	9.38	40.2
		6.54	10/ 9–10/10	4.89	3.5105	87.70	83.19	4.98	4.72	9.70	48.7
		6.56	10/10–10/11	4.89	3.7074	92.62	81.67	5.24	4.62	9.86	46.9
		6.63	10/11–10/12	4.89	3.8204	94.07	82.30	5.27	4.61	9.88	46.7
		6.67	10/12–10/13	4.89	3.8213	96.46	77.23	5.37	4.30	9.67	44.5
		6.68	10/13–10/14	4.89	3.6047	91.83	76.27	5.10	4.24	9.34	45.4
J. R.	2½ mo.	3.88	11/20–11/21	3.26	1.8578	57.73	28.91	5.52	2.77	8.29	33.4
		3.88	11/21–11/22	3.26	1.8356	48.29	21.38	4.62	2.05	6.67	30.7
	3 mo.	4.56	12/11–12/12	3.89	2.7641	65.81	63.09	5.36	5.14	10.50	49.0
		4.78	12/18–12/19	4.08	2.9479	69.46	61.91	5.39	4.81	10.20	47.2
	3½ mo.	4.88	12/26–12/27	4.08	2.8862	67.83	64.95	5.16	4.94	10.10	48.9
R. B.	4 mo.	7.32	2/12–2/13	4.70	2.7665	108.93	85.02	5.52	4.31	9.83	43.8
		7.32	2/13–2/14	4.70	2.8264	106.76	66.01	5.41	3.35	8.76	38.2
		7.42	2/19–2/20	3.75	2.6870	99.96	86.16	5.00	4.31	9.31	46.3
		7.42	2/20–2/21	3.90	2.5024	100.98	78.18	5.05	3.91	8.96	43.6
		7.42	2/21–2/22	4.17	2.3068	97.78	83.73	4.89	4.19	9.08	46.1
	5 mo.	7.84	3/12–3/13	4.70	2.8518	98.97	87.88	4.69	4.16	8.85	47.0
		7.84	3/13–3/14	4.66	2.9159	109.34	82.86	5.18	3.92	9.10	43.1
P. G.	3¼ mo.	5.90	2/19–2/20	3.64	2.1637	70.53	61.85	4.44	3.89	8.33	46.7
		5.90	2/20–2/21	3.64	2.3718	69.37	60.02	4.36	3.78	8.14	46.4
		5.90	2/21–2/22	3.64	2.2550	64.20	58.53	4.04	3.68	7.72	47.7
	3½ mo.	6.02	2/26–2/27	3.64	2.1725	66.26	64.57	4.09	3.98	8.07	49.3
		6.02	2/28–3/ 1	3.64	2.0335	63.78	57.12	3.93	3.52	7.45	47.2
	4 mo.	6.25	3/ 5–3/ 6	3.64	2.0320	63.11	58.88	3.75	3.50	7.25	48.3
		6.25	3/ 6–3/ 7	3.64	2.1335	67.86	53.06	4.03	3.15	7.18	43.9
		6.25	3/ 7–3/ 8	3.64	2.3594	69.37	62.90	4.12	3.74	7.86	47.6
W. W.	28 days	3.90	5/ 7–5/ 8	3.12*	1.5633	57.23	18.30	5.45	1.74	7.19	24.2
	29 days	4.02	5/ 8–5/ 9	3.12*	1.5996	54.37	19.50	5.02	1.80	6.82	26.4
M. M.	20 days	2.78	4/23–4/24	2.50*	1.3541	43.32	27.87	5.78	3.72	9.50	39.2
	21 days	2.88	4/24–4/25	2.50*	1.4124	42.99	26.32	5.54	3.39	8.93	38.0
	27 days	3.03	4/30–5/ 1	2.50*	1.2059	40.45	25.07	4.96	3.07	8.03	38.2
	28 days	3.06	5/ 1–5/ 2	2.50*	1.2626	42.74	26.77	5.19	3.25	8.44	38.5
R. S.	1 mo.	3.76	10/10–10/11	2.70	1.3158	49.65	3.03	4.90	0.30	5.20	5.8
		3.78	10/11–10/12	2.68	1.4032	49.49	5.79	4.86	0.57	5.43	10.5
		3.86	10/12–10/13	2.64	1.4611	50.46	6.86	4.85	0.66	5.51	12.0
		3.85	10/13–10/14	2.46	1.2566	48.40	10.55	4.67	1.02	5.69	17.9
		3.88	10/14–10/15	2.31	1.0662	46.74	11.78	4.47	1.13	5.60	20.2
		3.87	10/17–10/18	2.68	0.9651	48.09	6.85	4.61	0.66	5.27	12.5
		3.92	10/22–10/23	2.68	1.2940	49.98	8.93	4.73	0.85	5.58	15.2
		4.22	10/30–10/31	2.76	1.3238	50.28	4.57	4.42	0.40	4.82	8.3
		4.24	10/31–11/ 1	2.78	1.6398	58.80	5.85	5.15	0.51	5.66	9.0
		4.26	11/ 1–11/ 2	2.78	1.5412	56.43	7.37	4.92	0.64	5.56	11.3
T. G.	1½ mo.	4.09	9/18– 9/19	2.81	1.6507	58.59	30.97	5.32	2.81	8.13	34.6
		4.09	9/19– 9/20	2.73	1.6787	57.70	39.85	5.24	3.62	8.86	40.9
		4.03	9/20– 9/21	2.81	1.5908	57.48	43.53	5.29	4.01	9.30	43.1
		4.10	9/21– 9/22	2.81	1.4140	53.56	29.15	4.85	2.64	7.49	35.2
	2 mo.	4.54	10/ 3–10/ 4	2.81	1.7364	63.47	51.38	5.19	4.20	9.39	44.7
		4.60	10/ 4–10/ 5	2.81	1.7142	65.67	55.04	5.30	4.44	9.74	45.6
		4.62	10/ 5–10/ 6	2.81	1.7267	66.11	50.73	5.31	4.08	9.39	43.5

* This figure represents the nitrogen content of the food, but in these two infants (W. W. and M. M.) there were some vomiting and regurgitation almost every day.

He found marked fluctuations in the rate of excretion of both creatine and creatinine, especially the former. There appeared to be no regular time at which maximum and minimum rates of excretion consistently occurred. The total output for the day was usually approximately the same as that for the night. He found that the output of creatine paralleled the volume of urine but concluded that it may have been due in part to the large amounts of water which were given to ensure the obtaining of urinary specimens of adequate volume.

The diurnal variations in the output of creatine and creatinine of one infant have been studied over a period of seventy-two hours. The urine was collected as nearly as possible every four hours during the day and for twelve hour periods during the night. The results are presented in table 3. The marked fluctuations are obvious; their cause, less apparent. It is difficult to relate the variations to the ingestion of food, as Denis did for adults, since the infant received five identical meals at 6 and 10 a. m. and at 2, 6 and 10 p. m. It is of interest to note, however, that the total values for the day were always slightly greater than those for the night, when there was a longer interval between feedings (10 p. m. to 6 a. m.). It is also difficult to relate the output of creatine to periods of rest, as did Powis and Raper, since for the very young infant such periods are approximately the same during the day and night. No correlation was found between the volume of urine and the output of creatine, such as Rougichitch suggested. It seems probable that some of the fluctuation was due to the fact that the infant does not always empty the bladder completely at each voiding, so that there is frequently a variable amount of residual urine that escapes analysis in the period to which it belongs. The fact that the output of creatine varies so much for infants tends to invalidate conclusions drawn from experimental periods of short duration.

EFFECT OF AGE ON THE EXCRETION OF CREATININE AND CREATINE

Infants excrete less creatinine than adults. According to Amberg and Morrill,[19] the output of creatinine during the second week of life is small not only in the absolute sense but even in its relation to body weight, being only about one-third that of adults. All the infants studied in this series showed slightly larger amounts of creatinine than the work of Amberg and Morrill would lead one to expect. The creatinine coefficients varied from 3.75 to 5.78, values which are approximately one-half the coefficients for normal adults. The age range studied was small, varying only from 3 weeks to 7 months, but within that limited range age appeared to have no effect on the creatinine coefficients.

19. Amberg, S., and Morrill, W. P.: On the Excretion of Creatinine in the New-Born Infant, J. Biol. Chem. **3**:311, 1907.

Age plays a more important rôle in the output of creatine than in that of creatinine. The age at which the physiologic creatinuria of infancy and childhood disappears is somewhat indefinite. Apparently it diminishes gradually during later childhood and ceases at about the age of puberty. Several reports have indicated that in boys it may occasionally continue after that time (Rose,[20] Light and Warren [21]). The age of cessation of the creatinuria of girls is even less definite, and it is

TABLE 3.—*Diurnal Variation in the Urinary Excretion of Nitrogen, Creatinine and Creatine (R. B., Aged 5 Months, Weighing 7.9 Kg.)*

Date	Time	Length of Period, Min.	Urine, Cc.	Total Urinary Nitrogen, Gm.	Creatinine, Mg.	Creatine as Creatinine, Mg.	Rate per Twenty-Four Hours: Urine, Cc.	Nitrogen, Gm.	Creatinine, Mg.	Creatine as Creatinine, Mg.
3/19	10:15 a.m. to 2:18 p.m.	243	25	0.4163	16.08	13.74	148	2.4670	95.29	81.42
3/19	2:18 p.m. to 5:58 p.m.	220	38	0.4416	14.84	16.28	249	2.8905	97.16	106.56
3/19	5:58 p.m. to 10:05 p.m.	247	62	0.5966	20.74	16.24	361	3.4782	120.89	94.68
3/19	10:05 p.m. to 3/20 9:47 a.m.	702	189	1.3099	45.00	37.52	388	2.6870	92.31	76.96
	Total	1,412	314	2.7644	96.66	83.78	320	2.8198	98.58	85.44
3/20	9:47 a.m. to 2:07 p.m.	260	60	0.5157	20.41	14.81	332	2.8562	113.03	82.02
3/20	2:07 p.m. to 6:00 p.m.	233	71	0.4775	18.64	14.94	458	2.9511	115.17	90.33
3/20	6:00 p.m. to 10:10 p.m.	250	30	0.4851	17.58	13.25	173	2.7942	101.25	76.32
3/20	10:10 p.m. to 3/21 9:29 a.m.	679	198	1.4497	49.67	37.58	420	3.0745	105.34	79.70
	Total	1,422	359	2,9280	106.30	80.58	364	2.9590	107.64	81.60
3/21	9:29 a.m. to 2:10 p.m.	281	110	0.6080	22.53	20.96	564	3.1157	115.46	107.41
3/21	2:10 p.m. to 5:55 p.m.	225	68*	0.4282*	15.78*	12.34*	435*	2.7405*	100.99*	78.98*
3/21	5:55 p.m. to 8:00 p.m.	125	28	0.2502	8.92	6.77	323	2.8823	102.73	77.99
3/21	8:00 p.m. to 3/22 2:30 a.m.	390	64	0.8784	29.22	21.31	236	3.2433	107.89	78.68
3/22	2:30 a.m. to 10:05 a.m.	455	148	0.8953	33.33	25.40	468	2.8335	105.48	80.39
	Total	1,476	418*	3.0601*	109.78*	86.78*	408*	2.9855*	107.10*	84.66*

* Specimen incomplete owing to loss of one voiding. The maximum daily variation was: nitrogen, 36 per cent; creatinine, 28 per cent, and creatine, 35 per cent of daily average.

probable that this continuous creatinuria merges almost imperceptibly into the intermittent creatinuria that is normal in the adult woman.

The creatinuria of infancy begins at an early age, although there is evidence to indicate that it may not be present immediately after birth.

20. Rose, W. C.: Experimental Studies on Creatine and Creatinine: III. Excretion of Creatine in Infancy and Childhood, J. Biol. Chem. **10**:265, 1911.

21. Light, A. B., and Warren, C. R.: Creatinuria Among Adolescent Males, J. Biol. Chem. **104**:121, 1934.

Sedgwick [22] did not find any creatine in the urine of new-born infants during the first few days of life but subsequently found it in gradually increasing quantities. Amberg and Morrill [19] found creatine in the urine of an infant 13 days old. The youngest infants studied in this series were W. W., M. M., R. S., and T. G. An interesting point is at once evident from the data given in table 2, namely, that two of the infants (W. W., and R. S.) excreted very small amounts of creatine (creatine coefficients of 0.3 to 1.8), whereas the other two infants showed coefficients of approximately the same magnitude as those of the older infants. The explanation of this discrepancy presents difficulties. It cannot be explained entirely on the basis of age or weight

TABLE 4.—*Excretion of Creatinine and Creatine by Premature Infants* *

Case	Date of Birth	Birth Weight, Gm.	Date of Urinalysis	Time, Min.	Weight, Gm.	Creatinine, Mg.	Creatine as Creatinine, Mg.	Creatinine Plus Creatine, Mg.	Total Creatinine Excreted as Creatine, Percentage
1	4/ 5/34	1,080	6/11/34	†	2,900	5.87	0.34	6.21	5.5
			6/12/34	147	2,953	2.88	0.03	2.91	1.0
			6/13/34	180	2,964	3.30	0.24	3.54	6.8
			6/14/34	179	2,970	6.06	0.20	6.26	3.2
2	5/24/34	2,050	6/20/34	†	2,440	3.62	0	3.62	0
			6/21/34	209	2,444	4.80	0.15	4.95	3.0
3	7/ 6/34	2,220	7/11/34	†	2,128	5.40	0	5.40	0
			7/18/34	191	2,248	4.41	0	4.41	0
4	8/22/34	1,640	9/13/34	178	1,910	3.61	0	3.61	0
5	10/ 6/34	2,144	10/22/34	245	2,300	3.64	0	3.64	0
			10/24/34	205	2,309	3.98	0	3.98	0
			10/25/34	†	2,486	3.27	0	3.27	0
6	10/26/34	1,925	11/ 2/34	205	1,930	2.55	0.06	2.61	2.4
			11/ 3/34	203	1,926	3.62	0.05	3.67	1.4

* The infants received breast milk.
† The specimen was not timed, but the period was approximately three hours long.

because W. W., who showed a low coefficient, was older and heavier than M. M., who had a normal coefficient. All the infants were receiving protein in equal amounts on the basis of body weight, and all were gaining weight. All were normal full term infants.

This last point is of particular interest because premature infants have been shown to excrete little or no creatine. Paffrath and Ohm [23] studied five premature infants from 3 to 21 days of age and found creatinine coefficients of the same magnitude as for older infants but practically no creatinuria. Four other premature infants, aged from 4 to 7 months, excreted only from 6 to 14 per cent of the total creatinine in the form of creatine. A series of six premature infants studied here

22. Sedgwick, J. P.: Creatinine and Creatine Metabolism in Children, J. A. M. A. **55**:1178 (Oct. 1) 1910.

23. Paffrath, H., and Ohm, W.: Zur Frage der Kreatinurie des Frühgeborenen, Ztschr. f. Kinderh. **54**:377, 1933.

gave similar results, as may be seen from table 4. As twenty-four hour specimens were not collected, the coefficients could not be calculated for these infants, but it is obvious that during the short periods studied the infants excreted practically no creatine.

It is difficult to explain this anomalous behavior on the part of premature infants, but there are several possibilities that are worthy of consideration:

1. The capacity of the organism of premature infants to synthesize creatine may be markedly diminished or entirely absent. There is no evidence bearing on this point, but it is our intention to study the subject further by giving premature infants a substance, such as amino-acetic acid, which stimulates the production of creatine. This hypothesis, however, fails to explain the fate of the small amounts of creatine contained in the ingested milk.

2. The faculty inherent in the adult organism of converting creatine into creatinine may be enhanced in the premature infant. The fact that the creatinine coefficients of premature infants are approximately the same as those of older infants and only about half as large as those of adults tends to weaken this supposition.

3. Premature infants may be able to utilize or store creatine to a greater extent than are normal infants or children. It has been shown that an adult suffering from progressive muscular dystrophy has less than the normal amount of creatine in the muscles (Reinhold and his co-workers [24]) and that creatinuria is due to an inability to retain and utilize creatine in the muscles (Beard and his co-workers [25]). Hunter [5] thought that this defective capacity on the part of the muscles for the storage of creatine might be a contributory factor in the creatinuria of infants and children. It is conceivable that premature infants, in whom the building of muscle tissue presumably progresses at a greater rate than in children, are able to utilize all available creatine for this purpose and hence have none left to excrete. This theory is supported by work on adults with progressive muscular dystrophy. Several workers have found that when clinical improvement occurs during treatment with amino-acetic acid the creatinuria decreases, and Reinhold and his co-workers [24] found that the creatine content of the muscles increased at that time.

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24. Reinhold, J. G.; Clark, J. H.; Kingsley, G. R.; Custer, R. P., and McConnell, J. W.: The Effects of Glycine (Glycocoll) in Muscular Dystrophy with Especial Reference to Changes in Structure and Composition of Voluntary Muscle, J. A. M. A. **102**:261 (Jan. 27) 1934.

25. Beard, H. H.; Tripoli, C. J., and Andes, J. E.: The Diagnostic and Prognostic Significance of the Creatine-Creatinine Metabolism in Various Myopathies Before and After Amino-Acid Therapy, Am. J. M. Sc. **188**:706, 1934.

THE EFFECT OF DIET ON THE CREATINURIA OF INFANCY

In adults who do not excrete creatine the daily output of creatinine is remarkably resistant to changes initiated by dietary alterations.[26] This is also true of the excretion of creatinine of infants and children, as shown by Denis and Kramer,[16] Sawyer and his associates,[27] Gamble and Goldschmidt [28] and Talbot and Gamble.[29]

The excretion of creatine, on the other hand, can be markedly affected by diet. Denis and Kramer [16] found that in children it can be increased, diminished and even temporarily abolished by raising or lowering the consumption of protein. This was confirmed by Harding and Gaebler,[13] who found, however, that as the level of the ingestion of protein was raised, the output of creatine by children ultimately attained a constant maximum at a point at which the total creatine coefficient was the same as the creatinine coefficient of adults.

The effect of variations in the protein intake of infants on the excretion of creatine is more difficult to evaluate because the dietary protein for these subjects is furnished almost entirely by milk, which in itself contains creatine and creatinine. Thus an increase in the milk of the diet results in the ingestion of more creatine and creatinine with a consequent excess excretion of both substances, since they are largely excreted unchanged by the infant. Denis and Minot [30] found that the average value for creatinine in a large number of specimens of cow's milk was 1.15 mg. per hundred cubic centimeters and for creatine 1.91 mg.

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26. Shaffer.[14] Eimer, K.: Studien über den Kreatin-Kreatininstoffwechsel: I. Harn-kreatinin und Ernährung, Ztschr. f. d. ges. exper. Med. **74**:738, 1930. Deuel, H. J.; Sandiford, I.; Sandiford, K., and Boothby, W. M.: A Study of the Nitrogen Minimum: The Effect of Sixty-three Days of a Protein-Free Diet on the Nitrogen Partition Products in the Urine and on the Heat Production, J. Biol. Chem. **76**:391, 1928. Ringer, A. I., and Raiziss, G. W.: The Excretion of Creatinine by Human Individuals on a Prolonged Creatine-Free Diet, ibid. **19**:487, 1914. Terroine, E. F.; Bonnet, R.; Danmanville, P., and Mourot, G.: Contribution à la connaissance de la physiologie de la créatinine et de la créatine: I. L'excrétion de la créatinine et de la créatine dans la dépense azotée minima et dans l'inanition, Bull. Soc. chim. biol. **14**:12, 1932.

27. Sawyer, M.; Stevens, F. A., and Baumann, L.: Studies of Acid Production: I. The Varying Susceptibility of Children to Acidosis, Am. J. Dis. Child. **15**:1 (Jan.) 1918.

28. Gamble, J. L., and Goldschmidt, S.: A Study of Creatinuria in Infants: I. Relation of Creatinuria to Acidosis; The Elimination of Ingested Creatine and Creatinine: II. Relation of Protein Intake to Urinary Creatine, J. Biol. Chem. **40**:199 and 215, 1919.

29. Talbot, F. B., and Gamble, J. L.: The Protein Metabolism of an Infant, Am. J. Dis. Child. **12**:333 (Oct.) 1916.

30. Denis, W., and Minot, A. S.: The Non-Protein Nitrogenous Constituents of Cow's Milk, J. Biol. Chem. **38**:453, 1919.

In the experiments reported by Gamble and Goldschmidt [28] 300 cc. of milk (equivalent to 3.45 mg. of creatinine and 5.73 mg. of creatine) was added to the original diet. This dietary change resulted in a very slight change in the output of creatinine, from 79 to 82 mg. per day. The increase of 3 mg. might well have been caused by the increased ingestion of that substance. The creatine, on the other hand, increased from a rate of 59 to 100 mg. per day, a rise which certainly could not have been caused entirely by the additional creatine in the diet.

Since the effect of diet on the output of creatinine and creatine has been studied extensively and with concordant results, few such observations have been included in this investigation. Table 5 gives the results

TABLE 5.—*Effect of Dietary Changes on Excretion of Creatine (F. L., Aged 8 Months)*

Weight, Kg.	Date	Nitrogen Intake, Gm.	Total Urinary Nitrogen, Gm.	Creatinine, Mg.	Creatine as Creatinine, Mg.	Coefficient		
						Creatinine	Creatine	Total
6.36-6.74	10/ 4-10/14*	4.89	3.6138	91.86	73.23	5.22	4.16	9.38
7.25	11/ 6-11/ 7	6.53	4.1112	100.88	78.43	5.17	4.02	9.19
7.30	11/ 7-11/ 8	6.53	4.2566	103.23	84.30	5.25	4.29	9.54
7.40	11/ 8-11/ 9	6.53	3.9568	100.59	86.00	5.05	4.31	9.36
7.51	11/ 9-11/10	6.53	4.6390	109.73	130.34	5.42	6.44	11.86
	11/10	1.21						
7.53	11/13-11/14	0.97	1.8147	89.52	22.94	4.41	1.13	5.54
7.53	11/14-11/15	0.98	0.9369	83.50	36.13	4.12	1.78	5.90
7.53	11/15-11/16	0.96	0.5636	85.74	19.86	4.23	0.98	5.21

* Average of eight days on a normal diet (data in table 2). The diet during the foreperiod consisted of Klim, 120 Gm.; cane sugar, 42 Gm., and water, up to 1,000 Gm. The high protein diet consisted of Klim, 150 Gm.; cane sugar, 42 Gm.; water, up to 1,000 Gm., and cereal, 30 Gm. The low protein diet consisted of 40 per cent cream, 150 Gm.; dextrimaltose, 103 Gm.; water, up to 1,000 Gm., and cereal, 15 Gm.

of two short periods in one case. In the first period the protein of the diet was raised by increasing the amount of milk. This produced a marked increase in the excretion of creatine, which reached a maximum of 53 per cent more than the foreperiod level on the fourth day. At the same time a slight, probably insignificant, increase in the output of creatinine occurred. A low diet with a low protein content caused a marked diminution in the excretion of creatine, the lowest rate of excretion being 76 per cent below the foreperiod level. The excretion of creatinine decreased 19 per cent, the reduction being accounted for, in part at least, by the ingestion of a considerably smaller amount of creatinine. No parallelism between the fat and carbohydrate of the diet and the magnitude of creatinuria was observed for the different diets. These results are in complete agreement with the previously discussed results of other investigators.

THE FATE OF INGESTED CREATINE

Creatine ingested by healthy adults is not excreted in the urine unless the dose is greater than 1 Gm. per day (Folin,[31] Myers and Fine [32] and Rose and Dimmitt [33]). These earlier workers were also unable to find any evidence of an increase in the creatinine content of the urine and assumed that the ingested creatine was not converted into creatinine in the body. However, Benedict and Osterberg [34] were able to show that prolonged feeding of creatine to dogs resulted in an increase in the output of creatinine, which started at about the tenth day of the ingestion of creatine and reached its maximum in the ninth week. The total "extra" creatinine excreted accounted for 30 per cent of the ingested creatine. Rose, Ellis and Helming [35] repeated these observations on human beings, arriving at the same conclusion. They also recovered approximately one third of the ingested creatine as "extra" creatinine in the urine.

Infants and children, as well as many adults who have spontaneous creatinuria, have a very low tolerance for ingested creatine, a large proportion being excreted unchanged in the urine. Gamble and Goldschmidt [28] found that very small quantities of ingested creatine (12 to 16 mg. per kilogram per day) were enough to increase definitely the existing creatinuria of infants and that such ingested creatine was excreted far more completely than by adults. Other workers [36] confirmed these results in older children.

Table 6 gives the results of tests of creatine tolerance performed on five infants. Pure anhydrous creatine was given in the amounts noted.

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31. Folin, O.: The Chemistry and Biochemistry of Kreatin and Kreatinin, Festschrift für Olof Hammarsten, Uppsala, C. J. Lundström, 1906, pt. 3.

32. Myers, V. C., and Fine, M. S.: The Metabolism of Creatine and Creatinine: VII. The Fate of Creatine When Administered to Man, J. Biol. Chem. **21**:377, 1915.

33. Rose, W. C., and Dimmitt, F. W.: Experimental Studies on Creatine and Creatinine: VII. The Fate of Creatine and Creatinine When Administered to Man, J. Biol. Chem. **26**:345, 1916.

34. Benedict, S. R., and Osterberg, E.: Studies in Creatine and Creatinine Metabolism: V. The Metabolism of Creatine, J. Biol. Chem. **56**:229, 1923.

35. Rose, W. C.; Ellis, R. H., and Helming, O. C.: The Transformation of Creatine into Creatinine by the Male and Female Human Organism, J. Biol. Chem. **77**:171, 1928.

36. Powis, F., and Raper, H. S.[17] Magee, M. C.: Creatine and Creatinine Metabolism in Progressive Muscular Dystrophy: Report of Two Cases and Controls, Am. J. Dis. Child. **43**:19 (Jan.) 1932; Excretion of Creatine and Creatinine: Hourly Excretion in Normal Children and in Children with Progressive Muscular Dystrophy, ibid. **43**:322 (Feb.) 1932. Bodansky, M.; Schwab, E. H., and Brindley, P.: Creatine Metabolism in a Case of Generalized Myositis Fibrosa, J. Biol. Chem. **85**:307, 1929.

TABLE 6.—*Fate of Ingested Creatine*

Patient	Age Mo.	Age Days	Weight, Kg.	Date	Time	Ingested Creatine, Mg.	Nitrogen Intake, Gm.	Total Urinary Nitrogen, Gm.	Creatinine, Mg.	Creatine as Creatinine, Mg.	Coefficient Creatinine	Coefficient Creatine	Coefficient Total	Extra Creatine, Mg.	Recovery of Ingested Creatine, Percentage
J. R.	3	8	4.78	12/18–12/19	9:40 a.m. to 10:11 a.m.	...	4.08	3.0114	70.95	63.24	5.39	4.81	10.20		
	3	9	4.80	12/19	10:11 a.m. to 2:04 p.m.	300	....	0.3985	8.94	61.98	4.20	29.13	33.33	68.50	22.83
					2:04 p.m. to 6:05 p.m.	...	4.16	0.6228	14.32	69.08	6.62	31.92	38.54	77.41	48.64
					6:05 p.m. to 10:10 p.m.	...	....	0.2020	4.61	14.23	2.10	6.47	8.57	4.88	50.26
				12/19–12/20	10:10 p.m. to 9:48 a.m.	...	....	1.4939	33.19	63.13	5.30	10.07	15.37	43.66	64.82
	3	10	4.82	12/20–12/21	9:48 a.m. to 9:30 a.m.	...	4.08	3.1375	69.41	83.21	5.41	6.49	11.90	29.11	74.52
	3	11	4.84	12/21–12/22	9:30 a.m. to 10:09 a.m.	...	4.08	2.5215	70.46	62.25	5.26	4.65	9.91	0	74.52
J. R.*	3	16	4.88	12/26–12/27	2:30 p.m. to 9:12 a.m.	...	4.08	2.2488	52.85	50.61	5.16	4.94	10.10		
	3	17	4.90	12/27	9:12 a.m. to 2:20 p.m.	310	....	0.5857	12.67	71.05	4.49	25.17	29.66	75.35	24.31
					2:20 p.m. to 9:10 p.m.	...	4.17	0.7124	18.56	72.61	4.94	19.32	24.26	71.34	47.32
				12/27–12/28	9:10 p.m. to 9:15 a.m.	...	....	1.6207	39.19	59.77	5.90	8.99	14.89	35.68	58.83
	3	18	4.85	12/28–12/29	9:15 a.m. to 9:50 a.m.	...	4.08	2.9653	67.92	75.32	5.08	5.63	10.71	11.58	62.57
R. B.	3	23	7.32	2/12– 2/13	8:40 a.m. to 10:21 a.m.	...	4.70	2.9605	116.56	90.98	5.52	4.31	9.83		
	3	24	7.32	2/13– 2/14	10:21 a.m. to 9:45 a.m.	...	4.70	2.7557	104.09	64.36	5.41	3.35	8.76		
	3	25	7.32	2/14– 2/15	9:45 a.m. to 10:07 a.m.	...	4.70	2.1259	85.35	61.78	4.26	3.09	7.35		
	3	26	7.32	2/15	10:07 a.m. to 1:49 p.m.	310	....	0.4225	18.45	51.08	6.07	16.80	22.87	52.98	17.09
					1:49 p.m. to 3:27 p.m.	...	....	0.2189	8.67	34.37	6.46	25.61	32.07	38.97	29.66
					3:27 p.m. to 6:27 p.m.	...	4.79	0.3124	12.08	31.11	4.90	12.62	17.52	29.37	39.14
					6:27 p.m. to 9:40 p.m.	...	....	0.4028	14.08	26.33	5.33	9.96	15.29	22.23	46.31
			7.30	2/15– 2/16	9:40 p.m. to 9:25 a.m.	...	....	1.4345	52.82	79.32	5.49	8.24	13.73	58.98	65.33
	3	27	7.32	2/16– 2/17	9:25 a.m. to 8:45 a.m.	...	4.70	2.7623	108.82	107.45	5.68	5.61	11.29	51.12	81.82
R. B.	4	0	7.42	2/19– 2/20	9:50 a.m. to 9:42 a.m.	...	3.75	2.6721	99.40	85.68	5.00	4.31	9.31		
	4	1	7.42	2/20– 2/21	9:42 a.m. to 9:16 a.m.	...	3.90	2.4572	99.16	76.77	5.05	3.91	8.96		
	4	2	7.42	2/21– 2/22	9:16 a.m. to 9:43 a.m.	...	4.17	2.3500	99.61	85.30	4.89	4.19	9.08		
	4	3	7.40	2/22	9:43 a.m. to 12:49 p.m.	260	....	0.3320	14.30	29.85	5.55	11.59	17.14	25.27	9.72
					12:49 p.m. to 6:47 p.m.	...	4.50	0.6568	27.81	77.32	5.61	15.60	21.21	74.83	38.50
					6:47 p.m. to 10:20 p.m.	...	....	0.4210	16.35	28.52	5.55	9.67	15.22	21.47	46.76
				2/22– 2/23	10:20 p.m. to 9:19 a.m.	...	....	1.2528	50.07	67.90	5.49	7.44	12.93	39.63	62.00
	4	4	7.40	2/23– 2/24	9:19 a.m. to 10:00 a.m.	...	3.74	2.8528	113.90	100.98	5.56	4.93	10.49	21.01	70.08

R. B.	4	23	7.84	3/12– 3/13	9:58 a.m. to 10:05 a.m.	...	4.70	2.8657	99.45	88.31	4.69	4.16	8.85		
	4	24	7.84	3/13– 3/14	10:05 a.m. to 9:56 a.m.	...	4.66	2.8977	108.66	82.34	5.18	3.92	9.10		
	4	25	7.86	3/14	9:56 a.m. to 2:05 p.m.	260	....	0.6042	21.08	65.93	5.76	18.01	23.77	67.45	25.94
					2:05 p.m. to 5:00 p.m.	...	....	0.3359	12.32	34.49	4.79	13.40	18.19	31.79	38.17
					5:00 p.m. to 7:10 p.m.	...	4.69	0.2841	9.62	18.63	5.03	9.75	14.78	14.40	43.71
				3/14– 3/15	7:10 p.m. to 1:10 a.m.	...	....	0.7209	24.79	40.54	4.68	7.66	12.34	25.31	53.44
	4	26	7.86	3/15	1:10 a.m. to 9:28 a.m.	...	....	1.0493	38.24	48.81	5.22	6.67	11.89	25.42	63.22
	4	26	7.88	3/15– 3/16	9:28 a.m. to 10:12 a.m.	...	4.70	3.0000	107.58	111.17	4.92	5.08	10.00	30.56	74.97
P. G.	3	10	5.90	2/19– 2/20	10:25 a.m. to 9:39 a.m.	...	3.64	2.0046	68.28	59.87	4.44	3.89	8.33		
	3	11	5.90	2/20– 2/21	9:39 a.m. to 9:50 a.m.	...	3.64	2.3899	69.90	60.48	4.36	3.78	8.14		
	3	12	5.90	2/21– 2/22	9:50 a.m. to 9:35 a.m.	...	3.64	2.2315	63.53	57.92	4.04	3.68	7.72		
	3	13	5.92	2/22	9:35 a.m. to 1:54 p.m.	260	....	0.4193	12.50	49.47	4.36	17.25	21.61	50.96	19.60
					1:54 p.m. to 6:15 p.m.	...	3.71	0.4164	13.15	46.69	4.55	16.15	20.70	47.18	37.75
					6:15 p.m. to 10:00 p.m.	...	....	0.2880	8.67	16.49	3.48	6.62	10.10	9.35	41.34
				2/22– 2/23	10:00 p.m. to 9:24 a.m.	...	....	1.1079	33.21	56.61	4.39	7.47	11.86	36.97	55.56
	3	14	5.96	2/23– 2/24	9:24 a.m. to 10:10 a.m.	...	2.91	1.8881	62.97	85.55	3.80	5.16	8.96	30.97	67.47
P. G.*	3	27	6.25	3/ 5– 3/ 6	9:25 a.m. to 9:09 a.m.	...	3.64	2.0094	62.41	58.23	3.75	3.50	7.25		
	3	28	6.25	3/ 6– 3/ 7	9:09 a.m. to 9:30 a.m.	...	3.64	2.1646	68.85	53.83	4.03	3.15	7.18		
	3	29	6.25	3/ 7– 3/ 8	9:30 a.m. to 9:18 a.m.	...	3.64	2.3397	68.79	62.38	4.12	3.74	7.86		
	3	30	6.25	3/ 8	9:18 a.m. to 1:37 p.m.	260	....	0.5096	13.10	68.60	4.33	22.65	26.98	76.62	29.47
					1:37 p.m. to 6:07 p.m.	...	3.71	0.4540	14.10	49.42	4.47	15.66	20.13	50.74	48.99
					6:07 p.m. to 9:45 p.m.	...	....	0.3688	10.44	22.28	4.10	8.74	12.84	17.74	55.81
				3/ 8– 3/ 9	9:45 p.m. to 10:17 a.m.	...	....	0.9134	25.77	45.03	2.93	5.12	8.05	19.24	63.21
	4	0	6.27	3/ 9– 3/10	10:17 a.m. to 11:12 a.m.	...	3.64	2.4827	77.49	91.47	4.42	5.22	9.64	40.82	78.91
M. M.	0	20	2.78	4/23– 4/24	9:53 a.m. to 7:15 a.m.	...	2.50	1.2055	38.57	24.81	5.78	3.72	9.50		
	0	21	2.88	4/24– 4/25	8:30 a.m. to 10:02 a.m.	...	2.50	1.5026	45.74	28.00	5.54	3.39	8.93		
	0	23	2.88	4/26– 4/27	9:01 a.m. to 9:00 a.m.	200	2.55	1.2526	41.95	111.35	5.41	14.35	19.76	111.08	55.54
	0	24	2.94	4/27– 4/28	9:00 a.m. to 9:26 a.m.	...	2.50	1.2893	42.45	45.71	5.27	5.67	10.94	23.89	67.49
W. W.	0	28	3.90	5/ 7– 5/ 8	9:35 a.m. to 9:00 a.m.	...	3.12	1.5253	55.84	17.86	5.45	1.74	7.19		
	0	29	4.02	5/ 8– 5/ 9	9:00 a.m. to 8:45 a.m.	...	3.12	1.5829	53.80	19.30	5.02	1.80	6.82		
	0	30	4.00	5/ 9– 5/10	8:45 a.m. to 9:56 a.m.	200	3.17	1.5072	54.72	105.35	4.84	9.32	14.16	112.73	56.36
	1	0	4.00	5/10– 5/11	9:56 a.m. to 10:21 a.m.	...	3.12	1.5362	52.36	47.64	4.78	4.35	9.13	37.45	75.09
	1	1	4.08	5/11– 5/12	10:21 a.m. to 9:14 a.m.	...	3.12	1.5567	55.74	31.02	5.33	2.97	8.30	17.07	83.53

* Sodium benzoate given at the same time as creatine (table 9, experiments 6 and 7).

The creatine was always given at the same time of day (in the 10 a. m. feeding), since Powis and Raper [17] have expressed the belief that the utilization of creatine varies with the time of day at which it is given. In most instances the urine was collected every four hours for the first twelve hours after the ingestion of creatine, but the variations in such short periods have been shown to be so great (table 3) that in the later experiments only twenty-four hour specimens were analyzed. In no case was there a significant increase in the output of creatinine; so it may be concluded that none of the ingested creatine was converted into creatinine within the short periods studied (two or three days). The excretion of ingested creatine was fairly regular, from 55 to 65 per cent being excreted in the first twenty-four hours and a total of from 63 to 82 per cent in the first forty-eight hours. The average amount recovered was 60.7 per cent for the first twenty-four hours and 72.9 per cent for the first forty-eight hours. In most instances the excretion was not studied for more than forty-eight hours. In one case the excretion of creatine had reached the normal level in seventy-two hours, although only 74 per cent of the ingested dose had been excreted.

THE EFFECT OF INGESTION OF AMINO-ACETIC ACID

Spontaneous creatinuria occurs even when no creatine or creatinine is ingested, which indicates that creatine must be synthesized in the body. The fact that the magnitude of creatinuria, when present, can be altered by changing the intake of protein indicates that proteins or their metabolic products may be precursors of creatine. Harris and Brand [37] studied the effect of a large number of substances on the spontaneous creatinuria of patients with progressive muscular dystrophy and found that guanido-acetic acid and amino-acetic acid were capable of increasing the excretion of creatine. The pronounced effect of amino-acetic acid on creatinuria of patients with progressive muscular dystrophy was first reported by Brand, Harris, Sandberg and Ringer [38] and has since been confirmed by others (Thomas, Milhorat and Techner; [39] Kostakow

37. Harris, M. M., and Brand, E. : Metabolic and Therapeutic Studies in the Myopathies with Special Reference to Glycine Administration, J. A. M. A. **101**: 1047 (Sept. 30) 1933.

38. Brand, E.; Harris, M. M.; Sandberg, M., and Ringer, A. I.: Studies on the Origin of Creatine, Am. J. Physiol. **90**:296, 1929.

39. Thomas, K.; Milhorat, A. T., and Techner, F.: Untersuchungen über die Herkunft des Kreatins: Ein Beitrag zur Behandlung progressiver Muskelatrophien mit Glykokoll, Ztschr. f. physiol. Chem. **205**:93, 1932; Weitere Untersuchungen über die Herkunft des Kreatins, ibid. **214**:121, 1933. Milhorat, A. T.; Techner, F., and Thomas, K.: Significance of Creatine in Progressive Muscular Dystrophy and Treatment of this Disease with Glycine, Proc. Soc. Exper. Biol. & Med. **29**:609, 1932.

and Slauck;[40] Rutenbeck;[41] Cuthbertson and Maclachlan,[42] and Beard and his associates [25]). A similar effect on the creatinuria in cases of myasthenia gravis has been reported.[43] A preexisting creatinuria seems to be a prerequisite for this effect, because Zwarenstein,[44] Christman and Mosier [45] and Harris and Brand [37] observed no influence of this amino-acid on the output of preformed creatinine by normal adults nor did creatinuria result. On the other hand, amino-acetic acid does not necessarily increase an existing creatinuria. Cuthbertson and Maclachlan [42] gave 12 Gm. of amino-acetic acid a day to two normal children aged 12 and 14 years, but spontaneous creatinuria was not increased.

The effect of amino-acetic acid on the creatinuria of infants has been studied in this investigation, the results being presented in table 7 and chart. Relatively large amounts of amino-acetic acid are administered for therapeutic purposes, the usual dose for adults being from 10 to 20 Gm. per day. Harris and Brand [37] found that 7.5 Gm. per day almost always caused an increased creatinuria in patients suffering from progressive muscular dystrophy, but that larger doses were necessary to produce this effect in patients with neuromuscular conditions. In terms of body weight the effective dosage in cases of progressive muscular dystrophy ranged between 0.1 and 0.2 Gm. per kilogram. In an effort to find the minimum

40. Kostakow, S., and Slauck, A.: Die Glykokollbehandlung der progressiven Muskeldystrophie: Zugleich ein Beitrag zur Herkunft des Kreatins, Deutsches Arch. f. klin. Med. **175**:25, 1933; Ueber weitere Stoffwechsel-Untersuchungen mit Glykokoll bei progressiver Muskeldystrophie, ibid. **175**:302, 1933. Kostakow, S.: Die progressive Muskeldystrophie, ihre Vererbung und Glykokollbehandlung, Klin. Wchnschr. **13**:219, 1934.

41. Rutenbeck, H.: Studien über Glykokollelectrophoreses bei der Dystrophia musculorum progressiva, Klin. Wchnschr. **13**:1044, 1934.

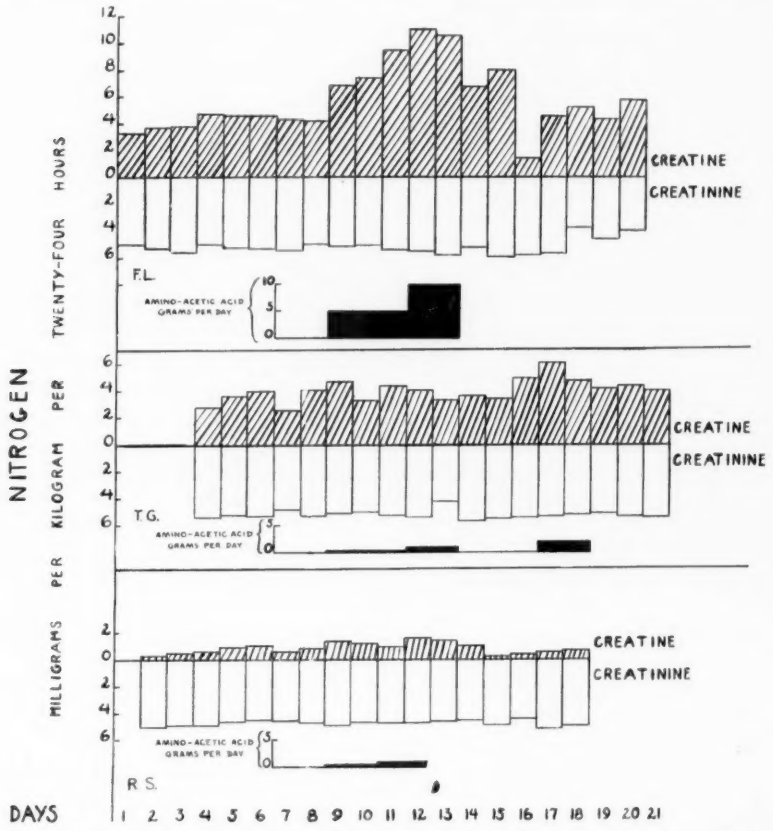
42. Cuthbertson, D. P., and Maclachlan, T. K.: The Treatment of Muscular Dystrophy with Glycine, Quart. J. Med. **3**:411, 1934.

43. Boothby, W. M. Myasthenia Gravis: A Preliminary Report on the Effect of Treatment with Glycine, Proc. Staff Meet. Mayo Clin. **7**:557 (Sept. 28) 1932. Boothby, W. M.; Adams, M.; Power, M. H.; Edgeworth, H.; Moersch, F. P.; Woltman, H. W., and Wilder, R. M.: Myasthenia Gravis: Second Report on the Effect of Treatment with Glycine, ibid. **7**:737 (Dec. 28) 1932. Boothby, W. M.: Myasthenia Gravis: Third Report on the Effect of Treatment with Glycine and Ephedrine, Arch. Int. Med. **53**:39 (Jan.) 1934; Fourth Report: The Onset and Course of the Disease, J. A. M. A. **102**:259 (Jan. 27) 1934. Remen, L.: Zur Pathogenese und Therapie der Myasthenia gravis pseudoparalytica, Deutsche Ztschr. f. Nervenh. **128**:66, 1932.

44. Zwarenstein, H. Studies in Creatinine and Uric Acid Metabolism: II. Ingestion of Proteins and Amino-Acids and the Hourly Elimination of Creatinine and Uric Acid, Biochem. J. **22**:307, 1928.

45. Christman, A. A., and Mosier, E. C.: Purine Metabolism: II. The Effect of the Ingestion of Glycine on the Excretion of Endogenous Uric Acid, J. Biol. Chem. **83**:11, 1929.

effective dose for infants, even smaller amounts were given at first. Five-tenths gram per day for two or three days caused a slight increase in the output of creatine, the maximum being 72 per cent more than the foreperiod level in R. S., and 45 per cent in T. G. Although the percentage of increase was impressive, the absolute amounts were scarcely significantly higher than some of the values obtained during the foreperiod. The dosage was therefore raised to 1 Gm. per day.



The effect of the ingestion of amino-acetic acid on the excretion of creatine and creatinine in the urine of infants.

This increased the excretion of creatine of R. S. to 110 per cent more than the foreperiod level, but had no such effect on T. G., the increase being only 35 per cent. T. G. was then given 2 Gm. per day for two days with a resultant maximum increase of 92 per cent.

It is obviously impossible to predicate a minimum effective dose from this small series of experiments, but it is apparent that an amount equivalent on the basis of weight to that effective in increasing creatinuria

TABLE 7.—*Effect of the Ingestion of Amino-Acetic Acid on the Excretion of Creatinine and Creatine*

Patient	Age Days	Date	Weight, Kg.	Amino-Acetic Acid Ingested, Gm.	Total Nitrogen Intake, Gm.	Total Urinary Nitrogen Gm.	Creatinine, Mg.	Creatine as Creatinine, Mg.	Coefficient		
									Creatinine	Creatine	Total
R. S.	30	10/10–10/11	3.76	...	2.70	1.3158	49.65	3.03	4.90	0.30	5.20
	31	10/11–10/12	3.78	...	2.68	1.4032	49.49	5.79	4.86	0.57	5.43
	32	10/12–10/13	3.86	...	2.64	1.4611	50.46	6.86	4.85	0.66	5.51
	33	10/13–10/14	3.85	...	2.46	1.2566	48.40	10.55	4.67	1.02	5.69
	34	10/14–10/15	3.88	...	2.31	1.0662	46.74	11.78	4.47	1.13	5.60
	37	10/17–10/18	3.87	...	2.68	0.9651	48.09	6.85	4.61	0.66	5.27
	42	10/22–10/23	3.92	...	2.68	1.2940	49.98	8.93	4.73	0.85	5.58
	43	10/23–10/24	4.00	0.5	2.85	1.3959	52.18	15.73	4.84	1.46	6.30
	44	10/24–10/25	4.06	0.5	2.86	1.5080	51.44	13.89	4.70	1.27	5.97
	45	10/25–10/26	4.06	1.0	3.00	1.4384	52.21	10.38	4.77	0.95	5.72
	46	10/26–10/27	4.10	1.0	2.95	1.5315	52.71	17.94	4.77	1.62	6.39
	47	10/27–10/28	4.14	...	2.74	1.4182	51.71	17.05	4.64	1.53	5.97
	48	10/28–10/29	4.16	...	2.75	1.3888	51.11	12.14	4.56	1.08	5.64
	49	10/29–10/30	4.20	...	2.72	1.3983	54.63	3.34	4.83	0.30	5.13
	50	10/30–10/31	4.22	...	2.76	1.3238	50.28	4.57	4.42	0.40	4.82
	51	10/31–11/ 1	4.24	...	2.78	1.6398	58.80	5.85	5.15	0.51	5.66
	52	11/ 1–11/ 2	4.26	...	2.78	1.5412	56.43	7.37	4.92	0.64	5.56
T. G.	55	9/18– 9/19	4.09	...	2.81	1.6507	58.59	30.97	5.32	2.81	8.13
	56	9/19– 9/20	4.09	...	2.73	1.6787	57.70	39.85	5.24	3.62	8.86
	57	9/20– 9/21	4.03	...	2.81	1.5908	57.48	43.53	5.29	4.01	9.30
	58	9/21– 9/22	4.10	...	2.81	1.4140	53.56	29.15	4.85	2.64	7.49
	59	9/22– 9/23	4.18	0.5	2.82	1.6875	59.10	46.43	5.25	4.12	9.37
	60	9/23– 9/24	4.19	0.5	2.91	1.7170	57.87	53.45	5.13	4.74	9.87
	61	9/24– 9/25	4.32	0.5	2.86	1.5872	57.72	38.11	4.96	3.27	8.23
	62	9/25– 9/26	4.32	1.0	3.01	1.7700	60.90	51.37	5.23	4.41	9.64
	63	9/26– 9/27	4.38	1.0	3.01	1.6793	63.52	48.76	5.38	4.13	9.51
	64	9/27– 9/28	4.42	...	2.78	1.3248	49.41	39.53	4.15	3.32	7.47
	65	9/28– 9/29	4.42	...	2.76	1.6071	67.09	43.31	5.63	3.64	9.27
	66	9/29– 9/30	4.46	...	2.81	1.5232	66.26	42.06	5.52	3.50	9.02
	67	9/30–10/ 1	4.46	2.0	3.21	1.8997	65.64	60.32	5.46	5.02	10.48
	68	10/ 1–10/ 2	4.46	2.0	3.21	2.0483	63.97	75.37	5.32	6.27	11.59
	69	10/ 2–10/ 3	4.56	...	2.81	1.7748	64.94	59.24	5.29	4.82	10.11
	70	10/ 3–10/ 4	4.54	...	2.81	1.7365	63.47	51.38	5.19	4.20	9.39
	71	10/ 4–10/ 5	4.60	...	2.81	1.7142	65.07	55.04	5.30	4.44	9.74
	72	10/ 5–10/ 6	4.62	...	2.81	1.7267	66.11	50.73	5.31	4.08	9.39
	Months										
F. L.	7	10/ 4–10/ 5	6.32	...	4.89	3.2801	84.65	55.90	4.97	3.28	8.25
		10/ 5–10/ 6	6.41	...	4.89	3.5009	90.76	64.10	5.23	3.71	8.94
		10/ 6–10/ 7	6.41	...	4.89	3.6650	90.78	65.14	5.61	3.77	9.38
		10/ 9–10/10	6.54	...	4.89	3.5105	87.70	83.19	4.98	4.72	9.70
		10/10–10/11	6.56	...	4.89	3.7074	92.62	81.67	5.24	4.62	9.86
		10/11–10/12	6.63	...	4.89	3.8204	94.07	82.30	5.27	4.61	9.88
		10/12–10/13	6.67	...	4.89	3.8213	96.46	77.23	5.37	4.30	9.67
		10/13–10/14	6.68	...	4.89	3.6047	91.83	76.27	5.10	4.24	9.34
		10/16–10/17	6.85	5.0	5.88	4.2210	95.45	127.56	5.17	6.90	12.07
		10/17–10/18	6.85	5.0	5.88	4.5578	94.61	135.54	5.13	7.35	12.48
		10/18–10/19	6.84	5.0	5.88	4.5107	100.42	172.36	5.45	9.35	14.80
	7½	10/19–10/20	6.84	10.0	6.86	5.3284	102.16	203.38	5.55	11.04	16.59
		10/20–10/21	6.89	10.0	6.86	5.4082	106.09	198.24	5.72	10.68	16.40
		19/21–10/22	6.94	...	4.11	3.2048	97.22	126.27	5.20	6.76	11.96
		10/22–10/23	6.90	...	4.89	3.7326	111.70	149.33	6.01	8.03	14.04
		10/23–10/24	6.70	...	4.30	3.0590	104.45	26.25	5.79	1.45	7.24
		10/24–10/25	6.60	...	2.71	2.7066	101.13	81.17	5.69	4.57	10.26
		10/25–10/26	6.60	...	2.84	1.8887	66.90	93.66	3.76	5.27	9.03
		10/26–10/27	6.59	...	3.86	2.2869	81.01	77.65	4.58	4.37	8.93
		10/27–10/28	6.69	...	4.89	2.5236	70.90	104.74	3.93	5.81	9.74

in adults suffering from muscular dystrophy is similarly effective in infants (0.5 to 1 Gm. per day; 0.1 to 0.2 Gm. per kilogram).

The behavior of R. S. is of particular interest. The excretion of creatine was extremely low and in this respect resembled that of an adult. However, the ingestion of amino-acetic acid increased the creatinuria, whereas no such effect has been observed in normal adults.

The effect of larger doses of amino-acetic acid was then studied. Five grams a day (0.73 Gm. per kilogram) was administered for three days to infant F. L. The dose was then increased to 10 Gm. a day for the next two days. It may be seen that there was an immediate and marked increase in the creatinuria. The augmentation in the output of creatine attained a height of 63 per cent more than the foreperiod level on the first day of the administration and reached a maximum of 165 per cent on the fourth day. When amino-acetic acid was no longer given, there was a gradual diminution to the normal level. The decrease was partially obscured in this infant by an infection of the upper respiratory tract and diarrhea, which began the day after the administration of amino-acetic acid was stopped.

Although the increase in the creatinuria in this case was comparatively large, the portion of ingested amino-acetic acid excreted as extra creatine was relatively small. Thus on the third day of the administration of amino-acetic acid to F. L. (Oct. 18 and 19) 98.42 mg. of creatine (expressed as creatinine) was excreted in excess of the basal rate. If 1 mol of creatine is equivalent to 2 mols of amino-acetic acid, this extra creatine would be equivalent to 131 mg. of amino-acetic acid, or only 2.6 per cent of the 5 Gm. ingested. Kostakow and Slauck [40] obtained similar results in cases of progressive muscular dystrophy. The maximum extra creatine was only from 400 to 450 mg. when 15 Gm. of amino-acetic acid was ingested. There was also a lack of proportionality between the amount of amino-acetic acid ingested and the extra creatine excreted, the increase resulting from 10 Gm. being much less than twice that from 5 Gm.

In all instances in which amino-acetic acid was fed to infants in this series, the effect on the excretion of creatine was negligible. This agrees with the results of Harris and Brand [37] obtained in cases of progressive muscular dystrophy. Thomas, Milhorat and Techner [39] as well as Kostakow anl Slauck [40] found that the excretion of creatinine tended to increase coincidentally with a decrease in the excretion of creatine after prolonged ingestion of amino-acetic acid. Whether or not this would occur in infants we are unable to say, as the administration of amino-acetic acid was not continued long enough.

THE EFFECT OF SODIUM BENZOATE [46]

Sodium benzoate is conjugated in the body with amino-acetic acid to form hippuric acid. It may also be conjugated with glycuronic acid, but it has been shown that in human beings the amino-acetic acid conjugation is the principal method of detoxication. In the one experiment in this series in which the total reducing substances of the urine were determined (table 8, experiment 1), there was no evidence that any ingested benzoate was excreted as glycuronic acid mono-benzoate. Quick [47] has shown that the amount of amino-acetic acid available in the body for the purpose of forming hippuric acid is definitely limited, and while it is synthesized, its formation is limited to the rate of approximately 9 mg. per kilogram an hour.

Our first problem was to determine the rate of synthesis of amino-acetic acid by infants. The procedure used by Quick [47] (collection of urine every one or two hours after the ingestion of benzoate) could not be followed here. It was necessary to analyze the urine as voided with the result that the periods immediately following the ingestion of benzoate varied in length from two hundred to three hundred minutes. Quick found that the maximum synthesis of amino-acetic acid as measured by the excretion of hippuric acid occurred approximately two hours after the ingestion of benzoate and that this level was maintained only as long as benzoate remained to be excreted. In selecting the dose of sodium benzoate, therefore, it was necessary to choose an amount which could not be excreted completely within five hours.

Thus, in experiment 3 (table 8), assuming that the infant was able to synthesize amino-acetic acid at the rate of 9 mg. per kilogram per hour, he should be able to excrete 371 mg. of sodium benzoate as hippuric acid in five hours. The dose used (600 mg.) was well above this figure and should theoretically have caused a maximum synthesis for at least five hours. If hippuric acid were always excreted at the same rate, it should require eight hours for the complete excretion of

46. Methods: Total reducing substances in the urine were determined by Benedict's method for blood sugar (Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry, Baltimore, Williams & Wilkins Company, 1932, vol. 2, p. 456) after preliminary treatment of the urine with specially prepared siliceous earth and permutit. Quick's method (Quick, A. J.: The Study of Benzoic Acid Conjugation in the Dog with a Direct Quantitative Method for Hippuric Acid, J. Biol. Chem. **67**:477, 1926) was employed for the determination of hippuric acid. This method when applied to normal urine always yielded a substance which reacted like hippuric acid. No attempt was made to identify this substance, but in calculating the recovery of benzoic acid a blank was subtracted which represented the amount of hippuric acid-like substance excreted during the fore-period.

47. Quick, A. J.: The Conjugation of Benzoic Acid in Man, J. Biol. Chem. **92**:65, 1931.

all the administered benzoate. It is probable, however, that the actual time required is somewhat longer than that, as there is a tendency for the rate of excretion to become less as the amount of benzoate to be excreted diminishes.[47] It will be seen in this experiment that amino-acetic acid was synthesized at a rate of from 8.4 to 8.8 mg. per kilogram per hour for seven hours after the ingestion of benzoate, a figure which compares favorably with Quick's result of 9 mg. per kilogram per hour. Repetition of this experiment three weeks later (experiment 6) gave a rate of 9.99 mg. per kilogram per hour, the only instance in which a rate greater than that predicted by Quick was obtained.

The next experiment of this series (4) was less enlightening because the dose of benzoate was too small to maintain the maximum synthesis of amino-acetic acid throughout the five hour period during which the urine was collected. It would be necessary to administer 535 mg. of

TABLE 8.—*Rate of Synthesis of Amino-Acetic Acid After the Ingestion of Sodium Benzoate*

Patient	Experiment Number	Date	Weight, Kg.	Sodium Benzoate, Mg.	Length of Period, Min.	Hippuric Acid, Mg.	Amino-Acetic Acid Equivalent, Mg.	Rate of Amino-Acetic Acid Synthesis, Mg. per Kg. per Hour
J. R.*	3	12/ 5	4.3	600	199	285.83	119.89	8.41
J. R.*	3	12/ 5	4.3	600	218	327.04	137.17	8.78
J. R.	6	12/27	4.88	600	245	474.75	199.12	9.99
P. G.	4	3/ 1	6.15	500	295	492.42	206.54	6.83
P. G.	7	3/ 8	6.25	500	256	520.07	216.13	8.18

* The first two periods represent two successive parts of one experiment.

sodium benzoate for this purpose, whereas only 500 mg. was administered. The lower rate of synthesis of 6.8 mg. per kilogram per hour was probably a natural sequence of this inadequate dosage. In experiment 7 the calculated amount of sodium benzoate necessary to cause a maximum synthesis during a period of two hundred and fifty-six minutes was 460 mg. The actual amount given was 500 mg., and the rate of synthesis (8.2 mg. per kilogram per hour) approached the theoretical value.

In general it may be said that, while it was impossible in this study to follow exactly the procedure outlined by Quick,[47] our results tend to confirm the applicability to infants of his hypothesis that adults are able to synthesize amino-acetic acid to conjugate benzoic acid at the rate of 9 mg. per kilogram per hour. Freiberg and West [48] found that it also applied to children with hypertrophic muscular dystrophy and Shorr,

48. Freiberg, I. K., and West, E. S.: Glycine Synthesis in Pseudohypertrophic Muscular Dystrophy, J. Biol. Chem. **101**:449, 1933.

Richardson and Wolff [49] found the same in adults with progressive muscular dystrophy and exophthalmic goiter.

The main object of this investigation, however, was not to determine the rate of synthesis of amino-acetic acid but to study the effect of depletion of body amino-acetic acid on the excretion of creatine. Since amino-acetic acid is a precursor of creatine, it is conceivable that its unavailability for the synthesis of creatine may cause a decreased excretion of creatine. Sodium benzoate was administered in order to divert amino-acetic acid to the synthesis of hippuric acid and thus render it unavailable for the formation of creatine. Harris and Brand [37] found that the administration of from 5 to 10 Gm. of sodium benzoate per day to adults with muscular dystrophy produced a prompt and appreciable decrease in the output of creatine.

The results of our study are shown in table 9. In the first experiment 300 mg. of sodium benzoate was ingested in one dose by J. R. This resulted in a 45 per cent decrease in the output of creatine in the following twenty-four hours. However, this decrease was apparently not regular because in the next experiment (2) there was an increase of 43 per cent. It was felt that these amounts of sodium benzoate were too small to be effective; so the doses were increased to 500 and 600 mg. The results of the next two experiments (3 and 4) were a decrease of 13 and 21 per cent, respectively, in the next twenty-four hours and of 36 and 9 per cent, respectively, in the following twenty-four hours.

There are several inherent difficulties in the interpretation of these results. In the first place the actual period of influence of benzoate is definitely limited, since it is excreted rapidly as hippuric acid at a rate equivalent to approximately 17 mg. per kilogram per hour of sodium benzoate. Thus, in experiment 1, in which 300 mg. of sodium benzoate was ingested, all should have been excreted in about four hours. Amino-acetic acid would be appropriated for the synthesis of hippuric acid, therefore, for only four hours out of the total twenty-four hour period. Any alteration in the excretion of creatine would have to be very large to be manifest under these conditions. The largest dose per unit of body weight was used in experiment 4, but even then only eight hours of synthesis of amino-acetic acid would be necessary to conjugate all the benzoate as hippuric acid.

In order to minimize this difficulty the urine was collected in short periods (as nearly four hour periods as possible) in order that the excretion of creatine might be determined during the actual time that amino-

49. Shorr, E.; Richardson, H. B., and Wolff, H. G.: Endogenous Glycine Formation in Myopathies and Graves' Disease, Proc. Soc. Exper. Biol. & Med. **31**:207, 1933.

TABLE 9.—*Effect of the Ingestion of Sodium Benzoate on the Excretion of Creatinine and Creatine*

Patient	Experiment No.	Age Mo.	Age Days	Weight, Kg.	Date	Time	Nitrogen Intake, Gm.	Total Urinary Nitrogen, Gm.	Creatinine, Mg.	Creatine as Creatinine, Mg.	Coefficient Creatinine	Coefficient Creatine	Coefficient Total	Hippuric Acid, Mg.	Benzoic Acid Equivalent, Mg.	Total Reducing Substances as Dextrose, Mg.	Medication Sodium Benzoate, Mg.	Medication Creatine, Mg.
J. R.	1	2	10	3.88	11/20–11/21	9:52 a.m. to 9:50 a.m.	3.26	1.8552	57.65	28.87	5.52	2.77	8.29	.....	.....	653		
		2	11	3.88	11/21–11/22	9:50 a.m. to 10:20 a.m.	3.26	1.8738	49.30	21.83	4.62	2.05	6.67	.....	.....	523		
		2	12	3.89	11/22–11/23	10:20 a.m. to 10:07 a.m.	3.26	2.0717	56.19	13.76	5.41	1.33	6.74	377.12	257.20	537	300	
		2	13	3.90	11/23–11/24	10:07 a.m. to 10:40 a.m.	3.26	2.0477	55.26	20.04	5.14	1.86	7.00	45.13	30.78		(10:05 a.m.)	
J. R.	2	2	17	4.08	11/27	10:18 a.m. to 2:32 p.m.	...	0.4261	10.04	7.30	5.18	3.76	8.94	260.59	177.73	...	326	
						2:32 p.m. to 9:55 p.m.	3.96	0.6119	15.34	9.21	5.25	3.15	8.40	31.83	21.71		(10:05 a.m.)	
					11/27–11/28	9:55 p.m. to 10:08 a.m.	....	1.3933	32.77	21.12	5.86	3.77	9.63	15.64	10.67			
		2	18	4.08	11/28–11/29	10:08 a.m. to 10:32 a.m.	4.08	2.5203	63.51	38.18	5.68	3.42	9.10	41.02	27.98			
J. R.	3	2	24	4.24	12/ 3–12/ 4	9:45 a.m. to 10:01 a.m.	4.08	2.5756	66.90	42.38	5.79	3.67	9.46	78.30	53.41			
		2	25	4.24	12/ 4–12/ 5	10:01 a.m. to 9:35 a.m.	4.08	2.3560	57.51	35.88	5.13	3.20	8.33	37.29	25.43			
		2	26	4.30	12/ 5	9:35 a.m. to 1:27 p.m.	....	0.3807	7.92	10.32	4.24	5.53	9.77	287.15	195.84	...	600	
						1:27 p.m. to 5:05 p.m.	4.08	0.4981	12.02	12.46	6.86	7.10	13.96	327.04	223.04		(10:08 a.m.)	
						5:05 p.m. to 10:27 p.m.	....	0.3873	10.15	3.84	3.92	1.48	5.40					
					12/ 5–12/ 6	10:27 p.m. to 9:32 a.m.	....	1.0544	24.27	12.86	4.54	2.40	6.94	50.31	34.31			
		2	27	4.30	12/ 6–12/ 7	9:32 a.m. to 10:13 a.m.	4.08	1.7242	46.75	27.86	3.92	2.34	6.26	53.05	36.18			
		2	28	4.40	12/ 7–12/ 8	10:13 a.m. to 10:27 a.m.	4.08	2.5490	59.74	56.60	4.99	4.73	9.72	45.29	30.87			
P. G.	4	3	6	6.02	2/26– 2/27	10:10 a.m. to 10:42 a.m.	3.64	2.2208	67.73	66.00	4.09	3.98	8.07	146.68	100.03			
		3	8	6.02	2/28– 3/ 1	10:15 a.m. to 9:20 a.m.	3.64	2.0039	61.35	54.94	3.93	3.52	7.45	82.19	56.05			
		3	9	6.15	3/ 1	9:20 a.m. to 2:15 p.m.	....	0.4917	13.75	17.67	4.05	5.21	9.26	492.42	335.83	...	500	
						2:15 p.m. to 6:48 p.m.	3.64	0.3585	10.63	9.13	3.38	2.91	6.29	40.69	27.75		(9:20 a.m.)	
						6:48 p.m. to 10:05 p.m.	....	0.2457	7.96	5.69	3.51	2.51	6.02	16.36	11.16			
					3/ 1– 3/ 2	10:05 p.m. to 10:02 a.m.	....	0.7522	22.84	18.13	2.77	2.20	4.97	27.94	19.06			
		3	10	6.15	3/ 2– 3/ 3	10:02 a.m. to 9:30 a.m.	3.64	1.9828	59.67	55.35	3.68	3.42	7.10	52.11	35.54			
J. R.	5	3	1	4.56	12/11–12/12	9:48 a.m. to 9:25 a.m.	3.89	2.7200	64.76	62.08	5.36	5.14	10.50	64.21	43.79			
		3	2	4.56	12/12–12/13	9:25 a.m. to 9:10 a.m.	4.08	2.8897	64.86	59.68	5.34	4.91	10.25	711.26	485.08	...	600*	
		3	3	4.60	12/13–12/14	9:10 a.m. to 9:10 a.m.	4.08	2.7406	61.93	57.40	5.00	4.63	9.63	705.02	480.82	...	600*	
		3	4	4.60	12/14–12/15	9:10 a.m. to 9:59 a.m.	4.08	2.9044	65.34	55.45	5.10	4.33	9.43	30.03	20.48			
		3	5	4.66	12/15–12/16	9:59 a.m. to 9:10 a.m.	4.08	2.8456	66.07	57.53	5.45	4.74	10.19	20.33	13.86			
J. R.	6	3	16	4.88	12/26–12/27	2:30 p.m. to 9:12 a.m.	4.08	2.2488	52.85	50.61	5.16	4.94	10.10	44.58	30.40			
		3	17	4.90	12/27	9:12 a.m. to 2:20 p.m.	....	0.5857	12.67	71.05	4.49	25.17	29.66	477.25	325.48	...	600	310
						2:20 p.m. to 9:10 p.m.	4.17	0.7124	18.56	72.61	4.94	19.32	24.26	185.07	126.22		(10:15 a.m.)	
						9:10 p.m. to 9:15 a.m.	....	1.6207	39.19	59.77	5.90	8.99	14.89	51.09	34.84			
					12/27–12/28	9:15 a.m. to 9:50 a.m.	4.08	2.9653	67.92	75.32	5.08	5.63	10.71	58.78	40.09			
		3	18	4.85	12/28–12/29													
P. G.	7	3	27	6.25	3/ 5– 3/ 6	9:25 a.m. to 9:09 a.m.	3.64	2.0094	62.41	58.23	3.75	3.50	7.25	110.13	75.11			
		3	28	6.25	3/ 6– 3/ 7	9:09 a.m. to 9:30 a.m.	3.64	2.1646	68.85	53.83	4.03	3.15	7.18	134.86	91.97			
		3	29	6.25	3/ 7– 3/ 8	9:30 a.m. to 9:18 a.m.	3.64	2.3397	68.79	62.38	4.12	3.74	7.86	132.12	90.11			
		3	30	6.25	3/ 8	9:18 a.m. to 1:37 p.m.	....	0.5096	13.10	68.60	4.33	22.65	26.98	520.07	354.69	...	500	260
						1:37 p.m. to 6:07 p.m.	3.71	0.4540	14.10	49.42	4.47	15.66	20.13	34.42	23.47		(9:21 a.m.)	
						6:07 p.m. to 9:45 p.m.	....	0.3688	10.44	22.28	4.10	8.74	12.84	14.79	10.09			
					3/ 8– 3/ 9	9:45 p.m. to 10:17 a.m.	....	0.9134	25.77	45.03	2.93	5.12	8.05	28.23	19.25			
		4	0	6.27	3/ 9– 3/10	10:17 a.m. to 11:12 a.m.	3.64	2.4827	77.49	91.47	4.42	5.22	9.64	9.79	6.68			

* Sodium benzoate was given throughout the day, 120 mg. being administered with each of five feedings. In all the other experiments the sodium benzoate was given in one dose with the 10 a.m. feeding at the exact time noted.

acetic acid was being diverted into hippuric acid. Even with this procedure it is impossible to draw conclusions because, as has been shown in an earlier section of this paper (table 3), the rate of excretion of creatine shows marked irregular diurnal variations when short periods are studied. However, it may be well to consider more in detail the three experiments (2, 3 and 4) in which this procedure was followed. In all there was an increase in the excretion of creatine during the period of from four to eight hours when amino-acetic acid was being used to conjugate benzoic acid. This was followed in every case by a sharp drop to below the foreperiod level. It is possible that this diminution in creatinuria represents a delayed effect of inadequate amino-acetic acid, but such a theory does not explain the initial increase. Terroine and his co-workers [50] found that the administration of large amounts of benzoic

TABLE 10.—*Relation of Creatine to Excretion of Nitrogen After the Ingestion of Sodium Benzoate* *

Experiment Number		Foreperiod Range	After Dose of Sodium Benzoate		
			First Period	Second Period	Third Period
2	Nitrogen	1.8 -2.5	2.4	2.3	...
	Creatine	2.49-3.42	3.76	3.15	...
3	Nitrogen	2.3 -2.5	2.3	3.3	1.7
	Creatine	2.69-3.20	5.53	7.10	1.48
4	Nitrogen	2.0 -2.2	2.4	1.9	1.8
	Creatine	3.52-3.98	5.21	2.91	2.51

* Nitrogen is expressed as grams per twenty-four hours; creatine, as milligrams of nitrogen per kilogram in twenty-four hours. All data concerning the dose of sodium benzoate, length of periods, etc., are given in table 9.

acid (5 Gm. per day) to growing pigs on a diet low in protein caused an increased creatinuria and an increased excretion of nitrogen, both of which they attributed to an increased destruction of body proteins initiated by the benzoic acid. This might also explain the initial increase in the creatinuria observed in our cases. As may be seen from table 10, there is a parallelism between the excretion of nitrogen and that of creatine after the ingestion of benzoate.

Shorr, Richardson and Wolff,[49] studying adults with progressive muscular dystrophy and with exophthalmic goiter, found significant increases in the excretion of creatine on the day that benzoate was administered. They suggest that this may have been due to the presence of increased amounts of amino-acetic acid in the blood stream preliminary

50. Terroine, E. F.; Bonnet, R.; Danmanville, P., and Mourot, G.: Contribution à la connaissance de la physiologie de la créatinine et de la créatine: II. L'excrétion de la créatinine et de la créatine au cours d'intoxications (acid benzoique, phlorhizoside, phosphore) provoquant une augmentation de la dépense azotée endogène, Bull. Soc. chim. biol. **14**:47, 1932.

to its conjugation with benzoic acid comparable to the effect of the ingestion of amino-acetic acid, or, what they consider more likely, it may have resulted from the loss of amino-acetic acid through the urine with an exacerbation of the primary defect in creatine metabolism.

In experiment 5 the benzoate was given in small doses throughout the day (120 mg. in each of the five feedings) for two days. This was followed by a steady decrease in the creatinuria, the excretion reaching a minimum of 16 per cent below the foreperiod level on the day after the administration of benzoate was discontinued.

In experiments 6 and 7 the problem was attacked from another point of view. The object was to test the reversibility of the reaction: amino-acetic acid $\rightleftarrows$ creatine. When the body is in acute need of amino-acetic acid, as it is after the ingestion of benzoate, can amino-acetic acid be formed from creatine? Sodium benzoate and creatine were administered together in the ratio of 1 mol of creatine to 2 mols of benzoate. The excretion of extra creatine was then compared with that noted in previous experiments in which the same dose of creatine without benzoate was given to the same infants (table 6). The first test (6) showed a suggestively lower recovery of creatine, but a repetition (7) on another infant did not confirm this, so it must be concluded that there was no definite evidence of a conversion of creatine to amino-acetic acid.

The effect of sodium benzoate on the creatinuria of infancy is apparently a double one. The fact that it causes an initial increase in the creatinuria may be attributed to an acceleration of the protein metabolism. The subsequent diminution in creatinuria may possibly be due to diversion to other purposes of amino-acetic acid ordinarily available for the synthesis of creatine. The net result of the ingestion of a single dose of sodium benzoate in the amounts used here on the twenty-four hour rate of excretion of creatine was usually a slight decrease. When the benzoate was given in divided doses throughout the day, the result was a slight but regular diminution in the creatinuria. This decrease is not as great as was observed by Harris and Brand [37] in adults, but the amounts of benzoate ingested were smaller.

COMMENT

Creatinuria, when naturally absent as it is in most adults, cannot be induced with facility. Therefore, investigations of the metabolism of creatine that are based on a study of its excretion in the urine must of necessity be carried out on subjects who show spontaneous creatinuria. Such subjects include normal infants and children, pregnant women and adults suffering from progressive muscular dystrophy, exophthalmic goiter and myasthenia gravis. There are a number of other conditions in adult life in which creatinuria occurs, but investigative work has

been confined for the most part to the diseases mentioned. Of this group only the creatinuria of infancy and childhood, the intermittent creatinuria of normal women and the regular creatinuria of pregnancy are considered physiologic; other types of creatinuria occurring in adults are generally thought to be pathologic. For this reason it might be supposed that studies on infants and children would be of particular value in investigating the problem of creatinuria. Unfortunately, as the studies presented here have shown, the creatinuria of infancy is irregular. It is true that normal infants excrete creatine, but the rate of excretion varies considerably even when relatively long periods (twenty-four hours) are compared. The fact that the rate of excretion of creatinine also fluctuates more than in the adult would indicate that the variation may be due in part to an incomplete emptying of the bladder by the infant at each voiding. However, irrespective of the reason, the fact is that the amounts of creatinine and of creatine excreted vary considerably from day to day for the same infant and such normal variations tend to minimize the significance of changes produced by experimental procedures. Changes of from 10 to 15 per cent above or below a foreperiod level certainly cannot be considered significant unless such small changes are consistently obtained.

Despite the fact that the infant is not an ideal subject for the investigation of creatine metabolism, many such studies have been carried out, and from them certain definite conclusions may be drawn. It is apparent that all normal infants and children after the neonatal period excrete creatine, such creatinuria ceasing usually at about the age of puberty. The amount of creatine excreted varies in different infants and is probably less, even in relation to body weight, during the first few weeks of life and as the age of puberty approaches. Premature infants apparently excrete little or no creatine.[23] Infants and children also excrete creatinine but in relatively smaller amounts and at a less constant rate than adults. The total creatine coefficient (creatine plus creatinine, expressed as milligrams of nitrogen per kilogram of body weight in twenty-four hours) of infants and children usually lie within the range established for the creatinine coefficient of adults, provided a suitable diet with an adequate amount of protein is employed.

The creatinuria of infancy and childhood is remarkably sensitive to experimental procedures. The output of creatine in the urine can be increased or diminished by appropriate changes in the protein level of the diet in the absence of alterations in the intake of creatine or creatinine as such. This indicates that creatine can be formed from protein or its metabolic products in the body. It has been pointed out that infants can form creatine readily from amino-acetic acid.

Creatine fed to subjects exhibiting spontaneous creatinuria is largely excreted unchanged. This apparently is true in all forms of creatinuria,

whether in infants or in adults. The infants studied in this series excreted about 61 per cent of the ingested creatine within twenty-four hours, with an added increment of 12 per cent in the succeeding twenty-four hours.

The pathogenesis of creatinuria has not been satisfactorily explained and there are many theories as to its causation. Hunter [51] gave the following tentative classification of creatinuria:

> In the absence of creatine in the diet, creatinuria is probably always endogenous. For its genesis in specific cases it is probable that any one or more of at least three different factors may be responsible:
>
> 1. The dissolution of creatine-containing tissue, as in starvation, carbohydrate privation and all states of negative nitrogen balance.
>
> 2. An excessive production of creatine, associated with the growth impulse as in childhood, or due to stimulation of endogenous metabolism as in fever, exophthalmic goiter or high-protein feeding.
>
> 3. A defective capacity on the part of the muscles for the storage of creatine, as in childhood and the muscular dystrophies.

Recent searches for the stimuli that initiate or inhibit creatinuria have led to a study of the influence of endocrine secretions. The fact that the creatinuria of childhood tends to disappear at about the age of puberty and that it reappears in senile persons and eunuchs led to the implication of the sex glands in its genesis. German investigators have been particularly active in this field. The hypophysis, because it furnishes a growth impulse during childhood, has also been considered. The importance of the secretion of the parathyroid glands in regulating calcium and phosphorus metabolism has long been recognized, and the suggestion has been made that it might affect creatine metabolism indirectly by its action on the phosphocreatine of muscles. The thyroid gland has also been shown to be intimately connected with creatine metabolism, since in cases of hypothyroidism no creatine is excreted even by children at ages when they would ordinarily show creatinuria, and the reverse is true in cases of hyperthyroidism. Adults with exophthalmic goiter excrete large quantities of creatine.

Studies of the effect of these endocrine products on the physiologic creatinuria of infancy and childhood are in progress in this laboratory at the present time and will be reported later. A discussion of the literature will be postponed until that time.

SUMMARY

A study of physiologic creatinuria and the influence of extraneous factors on such creatinuria was made on eight normal infants aged from 3 weeks to 7 months. The composite data were collected from a

51. Hunter,[5] p. 221.

total of one hundred and twenty-nine days. The results may be summarized as follows:

1. All the infants excreted creatine in the urine, the creatine coefficients (mg. of nitrogen per kilogram of body weight in twenty-four hours) varying from 0.3 to 5.14. The average value for infants over 1 month of age was 3.89. The coefficients ranged from 3.74 to 5.78, with an average of 4.93. The total creatine coefficients (creatinine plus creatine) ranged from 4.82 to 10.5 with an average of 8.86 for the group of infants over 1 month of age. With few exceptions the total creatine coefficients fell within the range of coefficients for preformed creatinine established for adults.

2. Age appeared to have no influence on the excretion of creatinine within the limited age range studied here (3 weeks to 7 months). Premature infants excreted practically no creatine, and this was also true for some very young full term infants. Various explanations for this failure to excrete creatine are discussed.

3. Creatinuria of infants could be diminished by feeding diets low in protein but of adequate caloric value. It could be increased by feeding diets high in protein. The excretion of creatinine was not materially affected by these changes in diet.

4. Infants have a low tolerance for ingested creatine. From 55 to 65 per cent of the amount ingested was excreted in the urine as creatine in the first twenty-four hours and 63 to 82 per cent in forty-eight hours.

5. The ingestion of amino-acetic acid increased the spontaneous creatinuria of infants but had no effect on the excretion of creatinine. Only a small fraction of the ingested amino-acetic acid was represented in the extra creatine excreted, and there was no specific quantitative relationship between the amount of amino-acetic acid ingested and the extra creatine excreted.

6. The effect of withdrawal of available amino-acetic acid from the body by diverting it to the formation of hippuric acid for detoxification of benzoic acid was studied. The ingestion of sodium benzoate causes an initial increase in creatinuria, due perhaps to the increased protein metabolism caused by the benzoate, followed by a decrease to below the foreperiod level.

An attempt has been made to evaluate the constancy of the normal creatinuria of infancy and to consider the effect of inherent variables, particularly age and diet, that might affect this creatinuria of infancy. The study forms a background for an investigation of the effect of endocrine products on creatinuria that will be reported subsequently.

THE SEVENTH NERVE AS A POSSIBLE PATHWAY FOR THE TRANSMISSION OF THE VIRUS OF POLIOMYELITIS

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I. CLINICAL OBSERVATIONS

The production of the spinal type of lesion usually seen in human beings with poliomyelitis can be best explained by assuming that the factor that causes the disease enters through the gastro-intestinal tract and from there spreads to the spinal cord by way of the sympathetic nervous system.[1] The production of the bulbar type of the disease may be explained by assuming that the virus can also spread from the gastro-intestinal tract to the medullary area by way of the axis-cylinders of both vagus nerves.[2] Symptoms of illness become evident as soon as the nucleus ambiguus is involved. The other cranial nerves, or components, especially the nuclei of the third, sixth, ninth and eleventh nerves situated in the medullary area, may also become involved, but only secondarily. Occasionally the nucleus of the seventh nerve becomes paralyzed along with the other nuclei. There are a few cases of the bulbar type, however, in which the only demonstrable finding is a lesion of the lower motor neuron of the seventh nerve. Occasionally, in a case in which there is primary involvement of the seventh nerve there will later develop involvement of the sixth nerve. At times paralysis of the seventh nerve may be associated with heterolateral hemispasticity. These instances of paralysis of the seventh nerve form a striking group of cases in which the mortality rate is low and the anatomic involvement limited and well marked. Obviously the same mechanism that produces the spinal and vagal types of the disease cannot effect solitary involvement of the nucleus of the seventh nerve.

It has been stated that the virus has merely an obligate affinity for naked gray fibers or axis-cylinders of medullated fibers.[1] Where in the gastro-intestinal tract are the naked gray fibers situated that could come in contact with the virus and absorb it? Besides the unmedullated

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1. Toomey, John A.: An Explanation of the Mechanism of Infantile Paralysis Production in the Human Being, Ann. Int. Med. **8**:854, 1935.

2. Toomey, John A.: Experimental Production of Bulbar Poliomyelitis, Proc. Soc. Exper. Biol. & Med. **32**:628, 1935; Poliomyelitis: II. The Bulbar Type, Am. J. Dis. Child., to be published.

terminal fibers of the olfactory nerve in the olfactory area there exist 1,600 or more cells of the unmedullated fibers of the terminal nerve. The nerve reaches of the latter, situated at the upper end of the stomodeum, cannot be differentiated from the nerve plexus of the gastro-intestinal tract, and morphologically, at least, they might be considered as being a part either of the intestine or of the sympathetic nervous system.[1] Absorption could take place here. Why could not nerves of a like type situated in the hindgut also absorb the virus of this disease?[1] Are there other indirectly exposed fibers in the intestine or its appendages? Each of the papillae or taste buds situated in the tongue has unmedullated fibers inside its cuplike excrescence. It is possible that the virus could be absorbed by the end-fibers of the chorda tympani nerve and pass by way of this nerve to the medullary area to involve the nucleus of the seventh nerve. It is likewise possible that the ninth nerve could absorb the virus.

Of 431 patients admitted to the division for contagious diseases of the City Hospital, 69 were classified as having bulbar lesions. Of this group, there were 45, 26 of whom died, in whom the lesion was of the vagal type.[2] The remainder, or 24 patients, had involvement of the facial nerves. (Through an error, one case was omitted from former computations.[2]) Eight of the 24 patients were ill with convulsions and 9 with vomiting; 6 had headache, 6 were constipated, 2 had diarrhea, 4 suffered from retention of urine, 5 had stiffness of or pain in the neck and 5 were delirious or semicomatose. The symptoms referable to the gastro-intestinal tract and to the nervous system were classified. Vomiting, constipation and diarrhea were considered referable to the gastro-intestinal tract; 14 of the 24 patients had either one or more of these symptoms. The second group of symptoms, those referable to the nervous system, included headache, delirium, dizziness, convulsions and coma. Twelve patients were included in this group, most of whom also had symptoms referable to the gastro-intestinal tract.

POSSIBLE ROUTES FOR THE SPREAD OF THE VIRUS

Group 1 (fig. 1).—The simplest type of lesions would occur if the virus of poliomyelitis spread by way of the chorda tympani nerve to the nucleus salivatorius adjacent to the nucleus of the seventh nerve. Such a spread occurred in 7 of the 24 cases in my series and involved only the seventh nerve. Two of the cases are described here.

B. P., aged 13 months, became ill on Oct. 1, 1931, with anorexia and fever. On October 2 he was drowsy, and his parents thought that he had a sore throat. On October 4, when he was admitted to the hospital, the left facial nerve was involved. The cell count of the spinal fluid was 73 per cubic centimeter; all of the cells were mononuclears. The temperature ranged from 38 to 39.5 C. (100.4 to 103.1 F.). The pulse rate was 120, and the respiratory rate, 20. On October 6

the temperature and the pulse and respiratory rates became normal, and by November 2 the paralysis of the muscles supplied by the seventh nerve had disappeared.

L. K., aged 5 years, became ill on July 1, 1927, with vomiting and pain in the back of the head. He was better the next day, but on August 10 the same symptoms recurred plus diarrhea. On August 24 paralysis of the right facial nerve developed, and the child was admitted to the hospital on August 31 in this condition. The temperature and the pulse and respiratory rates were normal. The cell count of the spinal fluid showed 50 cells per cubic centimeter, all of which were mononuclears. Eight years after the onset of the disease, in spite of all therapy, there were still slight palsy and some atrophy of the muscles supplied by the seventh nerve.

None of these 7 patients died; 2 could not be traced. One had slight and 1 complete residual facial paralysis after eight and one and one half years, respectively, while 3 recovered completely within a few weeks

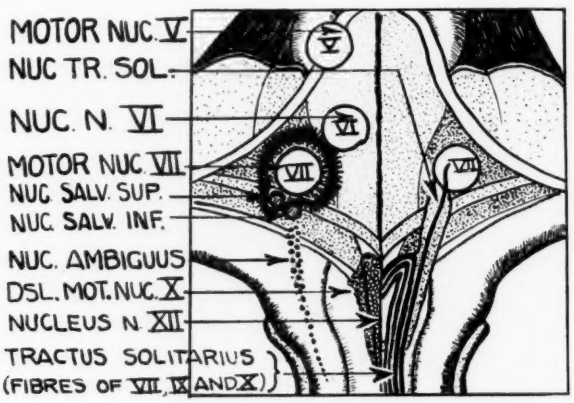

Fig. 1.—Schematic drawing showing the location of the lesion of poliomyelitis if the virus spread by the route indicated in group 1. In this and the following drawings the lesion is indicated by the area encompassed by the serrated line.

after the onset of the disease. The prognosis with regard to life seems excellent in this group of cases, and the chances for complete recovery of the nerve are better than 50 per cent.

Group 2 (fig. 2).—If the virus spreads along the axis-cylinders of the chorda tympani and seventh nerve to the nerve nuclei and spills over in the medullary area, the nucleus of the sixth nerve, because of its position, is most likely to be involved next. There were 2 such cases in this series, neither of which was fatal. One patient recovered completely from the effects of the paralysis, but after five years the other still has residual paresis of the muscles supplied by the sixth and seventh nerves.

A. M. T., aged 4 years, became ill on Sept. 18, 1928, with headache and vomiting. On September 20 he had convulsions and became semicomatose. On September 21 he was admitted to the hospital with a temperature of 39 C. (102.2 F.), a

pulse rate of 130 and a respiratory rate of 20. There was paralysis of the right facial muscles supplied by the sixth and seventh nerves. The spinal fluid contained 50 cells per cubic centimeter, 90 per cent of which were mononuclears. The temperature and the pulse and respiratory rates became normal on the third day of hospitalization, and there was complete recovery from the palsy of both nerves by October 8, the day of discharge from the hospital.

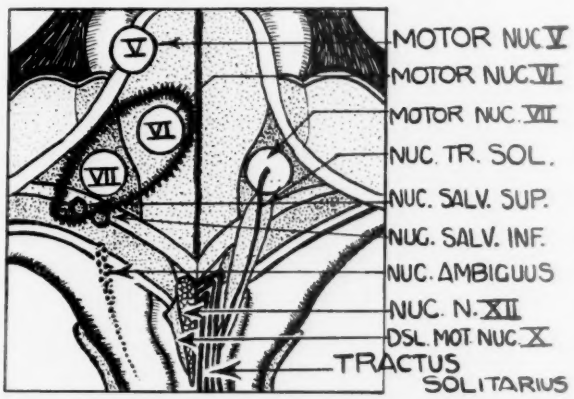

Fig. 2.—Schematic drawing showing the location of the lesion in group 2.

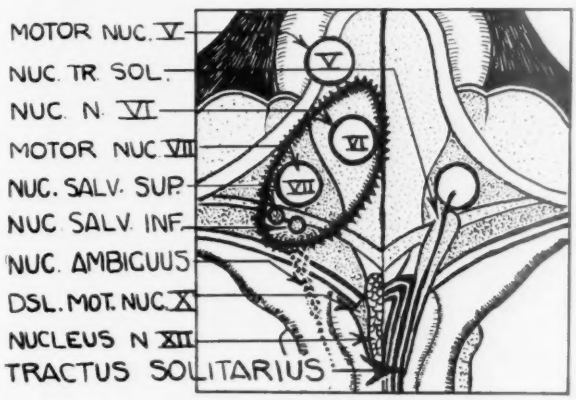

Fig. 3.—Schematic drawing showing the location of the lesion in group 3.

Group 3 (fig. 3).—If the virus spreads to the other cranial nuclei from the nucleus of the seventh nerve, the patient shows more objective evidence of disease and is more severely ill. Many of the homolateral cranial nuclei may become involved. There were 2 such cases in my series, 1 of which was fatal.

E. R., aged 4 years, became sleepy and feverish on Sept. 28, 1925. On September 29 he was still feverish and had a backache. He was admitted to the hospital on September 30, at which time he had paralysis of the muscles supplied by the right seventh nerve. The temperature was 38.3 C. (100.9 F.); the pulse rate, 92,

and the respiratory rate, 23. There were 112 cells in the spinal fluid, 95 per cent of which were mononuclears. Later that day the right external rectus muscle became involved. On October 1 there was an extension to the tenth nerve, as evidenced by dysarthria and dysphagia. Death occurred that night from bulbar palsy.

(It cannot be denied that in this case there may have been a concomitant absorption of the virus by way of both vagus nerves.)

Group 4 (fig. 4).—If the virus spreads to the nucleus of the seventh nerve, it may spill over and thus irritate the pyramidal tract. A crossed facial palsy would result. There were 6 such cases in my series; one of the patients died a few hours after admission. This case was not completely studied, and the diagnosis of tuberculous meningitis could

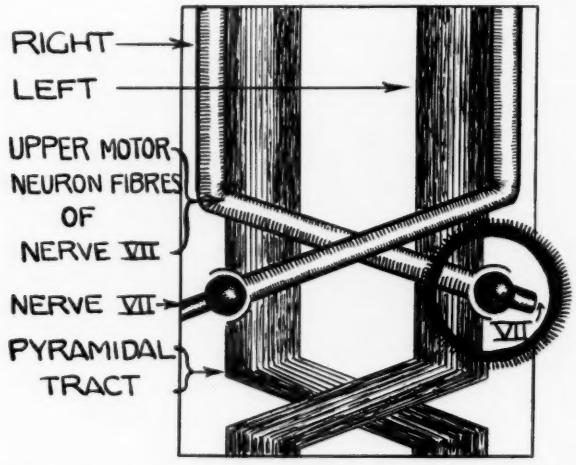

Fig. 4.—Schematic drawing showing the location of the lesion in group 4.

not be absolutely excluded. Of the remaining 5 patients, 3 recovered completely within a few weeks. Two recovered from the hemispasticity within two months, but 1 still had some facial weakness for five years and the other a year and a half after the onset of the disease.

R. K., aged 8 years, became ill on Aug. 28, 1933, with headache and anorexia. On admission to the hospital, on September 7, he had a stiff neck, painful muscles, paralysis of the muscles supplied by the left facial nerve and complete heterolateral spasticity on the right side. There was some questionable weakness of the hamstring muscles on the left side. The temperature was 37.9 C. (100.2 F.); the pulse rate, 115, and the respiratory rate, 20. There were 40 cells per cubic centimeter in the spinal fluid, 95 per cent of which were mononuclears. The child gradually recovered, and on discharge from the hospital, on March 14, 1934, he showed no evidence of spasticity, although there was still slight weakness of the muscles supplied by the left seventh nerve, a weakness which is still present.

M. A. W., aged 2½ years, became ill on Sept. 12, 1930, with lethargy and constipation. On September 16 she had convulsions. On September 17 her mother

noticed paralysis of the muscles supplied by the left facial nerve, and the child cried on being handled. On September 18 she had paresis of the muscles of the leg and retention of urine. On admission to the hospital, on September 22, the child had palsy of the left side of the face and spasticity of the right arm and leg. The temperature was 37.5 C. (99.5 F.); the pulse rate, 110, and the respiratory rate, 23. The spinal fluid contained 25 cells per cubic centimeter, all of which were mononuclears. The child recovered completely by October 14.

Group 5 (fig. 5).—The lesion of the seventh nerve may be associated with lesions of somatic nerve fibers of the spinal cord. The mechanism of the production of the latter has been explained previously.[1] It can be seen that if the virus is absorbed by any naked gray fiber it can simultaneously be absorbed from the lower and the upper part of

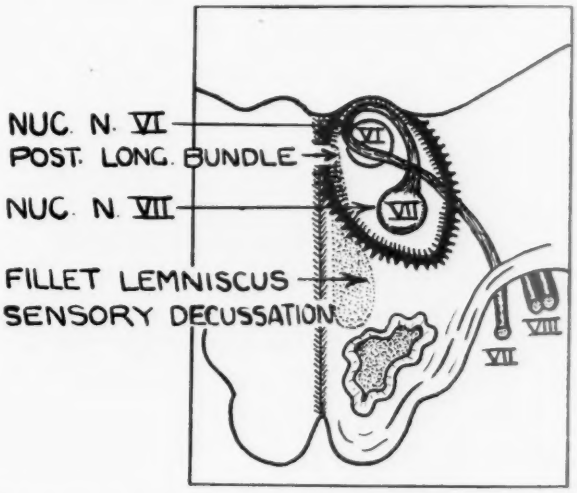

Fig. 5.—Schematic drawing showing the location of the lesion in group 5.

the gastro-intestinal tract. There were 6 patients with such lesions in my series, all of whom lived. The recovery of the muscles, however, depended on the amount of involvement in the spinal cord.

M. K., aged 7 years, became ill on Sept. 20, 1927, with headache, vomiting, constipation and fever. On September 21 her mother noted that something was wrong with the right side of the face. The patient had urinary retention. On admission to the hospital on September 22, she was drowsy and had paralysis of the muscles supplied by the right facial nerve. On September 23 there was an extension of the paralysis to the muscles supplied by the third, fourth and sixth nerves. On September 24 there was paresis of the quadriceps rectus muscle of the right leg. The pulse rate on admission was 110; the respiratory rate, 30, and the temperature, 39.5 C. (103.1 F.). The spinal fluid contained 69 cells per cubic centimeter, 95 per cent of which were mononuclears. By September 30 there was only weakness of the muscles supplied by the right facial nerve and of the quadriceps rectus muscle. The temperature became normal on this date, and the patient came out of her stupor. There was complete recovery from the paralysis of the quadriceps

rectus muscle in six months, but there is still a residual weakness of the facial muscles after eight years.

E. V., aged 13 years, became ill on Oct. 28, 1928, with headache, fever and vomiting. His illness was diagnosed as "flu." On October 29 he was restless. On November 1 he had cramps in the stomach and could not walk. On admission to the hospital on November 2 the urinary bladder was found to be paralyzed; there was complete paralysis of both arms and legs, and the muscles supplied by the right facial nerve were involved. The cell count of the spinal fluid was 175 per cubic centimeter, 90 per cent of the cells being mononuclears. The child was discharged on request on December 23, although he still had paralysis of both legs and the right facial muscles.

The following case history may be given since it illustrates the anatomic response one would expect with any noxious agent which spreads from the nucleus of the seventh nerve to the pyramidal tract, the nucleus of the sixth nerve and posterior longitudinal bundles. Such a syndrome could be styled a modified Foville syndrome.

M. M. S., aged 4½ years, became ill on Oct. 24, 1934, with malaise and anorexia. On October 25 she had pain in the stomach. On October 26 she vomited and still complained of abdominal pain. On October 27 she complained of pain in the legs, which was more severe on the right side. On October 28 she was unable to stand. On admission to the hospital, on October 29, the temperature and the pulse and respiratory rates were normal. There were practically complete paralysis of both lower extremities, weakness of the right facial and right external rectus muscles, a failure of conjugate deviation to the right and a deviation of the tongue to the right, with marked signs of meningeal irritation. There was no hemispasticity. There were 60 cells in the spinal fluid per cubic centimeter, all of which were mononuclears, and the Pandy reaction was 4 plus. On October 30 there was a droop of the left eyelid and some questionable dysphagia. By November 13 all of the muscles supplied by the cranial nerves had become normal. By December 24 the child had recovered completely.

COMMENT

Although the virus of poliomyelitis may be absorbed by any gray nerve fiber the production of the clinical condition called poliomyelitis depends on the size of the absorbing nerve fiber and the nearness of it to the central nervous system. Although the skin contains gray fibers it would take thousands of minimal paralyzing doses of the virus to produce the effect that a single dose of the same amount would produce after intracerebral injection into a monkey. The length of the chorda tympani nerve, the small size of this nerve, the fact that it is medullated and its devious course to the medullary area are factors that would tend to retard the virus from spreading to the medullary area. Many taste buds might absorb the virus and yet the disease might not be produced, since the virus might be absorbed and its spread checked somewhere between the peripheral absorbing area and the nucleus of the nerve. Obviously, there are fewer cases in which the

seventh nerve is involved than there are cases in which the spinal nerves are involved. Experimentally, however, such an entity can be produced in the Macacus rhesus monkey, as noted in the second part of this paper.

It cannot be said that this method of spread is entirely hypothetic, since I have been able to produce the same condition experimentally in the M. rhesus monkey when this avenue of approach was used. Nor can it be said that there is no possibility of absorption from the taste buds on the ground that there are no exposed fibers as there are in the olfactory area. In the monkey the nerve fibers are not exposed in the intestines either, and normally the virus is washed through the intestine. It is only when the virus can approximate the gray fibers by dilating the intestine that the disease follows. Many things could cause natural distention. Analogously, although I punctured the taste buds to achieve my purpose, I was able to demonstrate a condition in the experimental animal similar to that which appears in the human being. Further work is necessary to show under what conditions the approximation of the virus occurs naturally.

I have purposely not mentioned the type of absorbing fiber, since the virus of poliomyelitis has no selective affinity for afferent or efferent pathways as such. It is absorbed by any gray fiber and runs dromically or antidromically to the physiologic direction of flow of the nerve impulse.

In my figures the tractus solitarius is not shown. In Wright's textbook,[3] one finds the statement that "the connector fibers . . . pass to Meckel's ganglion, etc. . . . to end about the ganglion in the vicinity of the submaxillary and sublingual glands. As the pars intermedia conveys taste fibers from the anterior two thirds of the tongue to the superior salivary nucleus, another reflex arc for the secretion of saliva becomes evident."

One might object to my interpretation of cross facial paralysis, thinking in terms of absorption. The axis-cylinders can be compared to a railway system, the nerves being the railroad tracks on which the virus, the engine, runs in order to reach its end-stations, the cells of origin. Here it is transferred if it is to travel farther. Were it not stopped at this point one would have a lower motor neuron response of the facial nerve on the same side as the lesion and a homolateral hemispasticity. But there is a lower motor neuron response on the same side as the lesion and a heterolateral hemispasticity in these cases. The

3. Wright, Samson: Applied Physiology, ed. 3, New York, Oxford University Press, 1929.

only logical explanation is to suppose that the pyramidal tract is irritated, as indicated in figure 4. There is a common comparative condition due to a vascular disturbance in this area. Since poliomyelitis in its later stages, at least, is a disease with marked cuffing and perivascular infiltration with lymphocytes and at times actual focal clusters of red cells, it is not illogical to suppose that these irritative conditions in this anatomic location could bring about the clinical picture one sees.

CONCLUSIONS

The production of the isolated paralyses of the muscles of the seventh nerve that occur as a result of poliomyelitis can be best explained by assuming that the portal of entry is by way of the gastro-intestinal tract; in this instance, via the gustatory fibers.

II. EXPERIMENTAL OBSERVATIONS

In Macacus rhesus monkeys the seventh nerve was exposed at the stylomastoid foramen and stripped back to the first large bifurcating branch. All operations were done with the monkey under complete ether anesthesia. The effect of irritation was tested in two animals by crushing the nerve three times with a hemostat. Slight paresis resulted, but complete recovery occurred forty-eight hours later. The effect of crushing the seventh nerve and then injecting a solution into it was tested on two animals. When the nerve was crushed three times, as described, and 0.2 cc. of a 1 per cent solution of the virus of poliomyelitis injected into it, the immediate effect was not marked, but when 0.3 cc. of the same virus solution was injected along the course of the nerve, complete unilateral peripheral paralysis of the seventh nerve was produced immediately. The production of this immediate paralysis was not due to the virus itself, for when two other animals were given injections of the same amount of saline solution in the same way paralysis was immediately produced. No central effect was observed in sections of the nuclear area of the seventh nerve. Whether immediate paralysis was caused by the virus or the saline solution, the results were the same, recovery occurring in from forty-eight to seventy-two hours. In the following experiments the injections were made into the left seventh nerve after it was crushed as described.

Animal 1 was given an injection of 0.2 cc. of a 1 per cent solution of the virus. There was no effect, save furring which occurred on the seventh day after the injection. Animal 2 was given an injection of the same amount of the virus solution as animal 1. Weakness of the left side of the face developed on the third day, paresis of the left foot on the fifth day and diarrhea on the tenth day. There were no further developments. Animal 3 was given an injection of 0.3 cc. of a 10 per cent solution of the virus; on the fourth day after the injection there was furring, and the left arm was weak; on the fifth day the muscles supplied by the left facial and the left abducens nerves were paralyzed as well as both arms and legs, and there was incoordination of the movements of the eyeballs; on the seventh day the animal was completely paralyzed and died. Animal 4 was given an injection of the same amount of virus solution as animal 3. There was furring on the fifth day; on the sixth day he could not close the left eyelid; on the twelfth day he regained the ability to close it, and there were no

further signs or symptoms. Animal 5 was given the same dosage of virus solution as animal 2. Facial paralysis developed on the left side immediately after the injection; on the fifth day there was edema of the face; on the eighth day, furring, and on the tenth day, questionable weakness of the left foot. There were no further signs or symptoms. Animal 6 was given the same dosage of virus solution as animal 3. Facial paralysis developed on the left side immediately after the injection; on the second day there were some facial edema and furring; on the sixth day the animal could not use the left external rectus muscle. There was incoordination of the movements of the eyeballs. That there was a nuclear lesion of the sixth nerve was obvious, since there was weakness of the opposite internal rectus muscle. The head drooped forward, and both arms, but neither leg, were paralyzed. The next day the legs became paralyzed. The animal was killed, and sections were made on the ninth day. Animals 3 and 6 presented exact duplicates of the clinical type of case seen in the human being.

Although the exact clinical condition seen in the human being was reproduced in the Macacus rhesus monkey, it was obvious that the method of introduction of the virus was highly artificial. It was decided to introduce the virus into the tongue through the taste buds of the chorda tympani. Even here, it was impossible to avoid overabsorption by gray fibers of the fifth, ninth and tenth nerves, but it was thought that even if this did occur enough virus might be absorbed by the fibers of the chorda tympani to produce an occasional local response in the nucleus of the seventh nerve. All injections were made into the right anterior two thirds of the tongue. A fine needle was used, and care was taken to pierce each taste bud on that side. The pharynx was blocked by gauze to avoid regurgitation of the virus, which otherwise might thus approximate the olfactory area. In preliminary experiments attempts were made to inject the virus just underneath the outer layer of epithelium, with no great success. Since some virus could escape by that method, there was a possibility that the olfactory area might become infected. For this reason the virus was injected through the taste buds into the substance of the tongue without losing any of it.

Animal 7 was given an injection of 2 cc. of a 1 per cent solution of the virus with no results. Animal 8 received an injection of the same amount. Nine days later he had facial palsy on the right side and paralysis of both upper extremities. He was able to swallow and to cry out clearly. Later that day his voice became hoarse. On the tenth day he showed further involvement of the vagus nerve in that he had dysarthria and dysphagia. He still had facial palsy on the right side, and the legs were becoming weaker. That night he was completely paralyzed, and died the next day. Animals 9, 10 and 11 were each given 3 cc. of a 1 per cent solution of the virus. Only one had a questionable weakness of the muscles supplied by the right facial nerve five days later. Animals 12, 13 and 14 were given 2 cc. of a 1 per cent solution. Animal 14 died the day after the injection. Autopsy showed marked gastro-enteritis, but nothing specific. Animals 15 and 16 were given 3 cc. of a 10 per cent solution of the virus. Animal 15 had involvement of the right sternocleidomastoid muscle and the right facial muscles with some dysarthria and dysphagia on the sixth day. Mucus drooled from the mouth, and both arms were weak. There was a definite tremor, but the legs were not involved. The legs were weaker on the seventh day, and the animal had complete quadriplegia. He died on the eighth day after the injection. Animal 16, although active, had involvement of the right facial muscles, slight dysarthria and furring on the sixth day. He could swallow. His condition remained about the same

on the seventh and eighth days. On the ninth day he had a generalized coarse tremor, and both upper extremities were paralyzed, although the legs were unaffected. There were facial palsy on the right side and some edema of the face and neck. Later the same day both upper extremities and the right lower one were paralyzed, and there was marked dysphagia. On the tenth day complete quadriplegia developed, and the animal died.

These experiments suggest that the virus can travel along the chorda tympani to the superior salivary nucleus and from thence to the nucleus of the seventh nerve in the medulla.

OBSTRUCTIVE PULMONARY EMPHYSEMA DUE TO PARTIAL OBSTRUCTION OF THE BRONCHI BY TUBERCULOUS LESIONS

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Probably nowhere in medicine is a cause and effect relationship between a given lesion and the resulting clinical picture more clearly demonstrable and predictable than in the case of partial or complete obstruction of a bronchus. Most of the exact knowledge on the subject is found in the epochal work of Chevalier Jackson. While such a relationship is most evident when the obstruction is due to the presence of a foreign body, conditions arise within the organism itself that can be evaluated with like accuracy. It is the purpose of this paper to report on a series of patients in whom tuberculous lesions of various kinds produced the characteristic clinical picture that results from partial obstruction of a main bronchus.

Obstruction to a major bronchus may be complete or partial. If the obstruction is complete, ventilation of the affected side ceases and the air in the alveoli is absorbed [1] or pumped out.[2] The lung then passes into a state of collapse or atelectasis.

If the obstruction is incomplete, an entirely different end-result occurs. Instead of atelectasis emphysema will ensue, the presence of which may be explained as follows: 1. The obstruction may be so peculiarly constituted that a true valve occurs, allowing air to go in but not out. A polyp or a flaplike tumor might cause this.[1c] 2. The bronchi change size during respiration, becoming wider and longer during inspiration and narrower and shorter during expiration.[3] Under these con-

Read before the Chicago Pediatric Society on Feb. 19, 1935.

From the service of Dr. Joseph Brennemann, the Children's Memorial Hospital.

1. (*a*) Fuchs, C. F.: Die Bronchitis der Kinder, Leipzig, O. Wigand, 1849. (*b*) Lichtheim: Versuche über Lungenatelektase, Arch. f. exper. Path. u. Pharmakol. **10**:54 (Dec.) 1878. (*c*) Jackson, C.: Mechanism of Physical Signs in Neoplastic and Other Diseases of Lung, with Especial Reference to Atelectasis and Emphysema, J. A. M. A. **95**:639 (Aug. 30) 1930.

2. Jackson.[1c] Gairdner, W. T.: On the Pathological Anatomy of Bronchitis and the Diseases of the Lung Connected with Bronchial Obstruction, Month. J. M. Sc. **11**:122 and 230, 1850.

3. Gottstein, G.: Diagnose und Therapie der Fremdkörper in den unteren Luftwegen, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **30**:279 (supp. 3) 1907. Francis, B. F.: Changes in the Shape and Size of the Tracheobronchial Tree Following

(Footnote continued on next page)

ditions a verrucous or polypoid lesion might allow air to pass in during inspiration, when the bronchus had a larger cross-section, but would impede the expiration when the cross-section became smaller. 3. When breathing is interfered with mechanically, inspiration is at first prolonged,[4] made deeper and more forceful, while expiration is practically unchanged. As a consequence, air is trapped behind the obstruction [5] after each inspiration, and the end-result is overdistention of the affected lung.

The problem of detection of obstructive emphysema is not difficult. Dyspnea and cyanosis may be present, depending on the extent of the emphysema. If the emphysema is of low grade, there may be no dyspnea and no cyanosis; but in the severe forms, in which the ballooning out of the affected lung results in impaired function on the affected side and in atelectasis of the normally functioning lung from pressure, cyanosis and dyspnea may be quite intense. The cry which occurs with the latter condition is typical of that indicating limited vital capacity. The wail is short-lived and gives one the impression that it would be longer if more air were available.

An asthmatoid wheeze may be heard at the open mouth during expiration.[6] At times, the wheeze may be scarcely heard during normal breathing. In deep breathing or in clearing the bronchi of secretion its audibility may increase. This expiratory difficulty associated with asthmatoid wheeze was noted by Schick with reference to tuberculosis of the hilar glands.[7]

On examination, the affected side shows a large hemithorax, widening of the intercostal spaces, limitation or absence of respiratory movement, displacement of the heart to the opposite side, hyperresonance,

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Stimulation of the Vagosympathetic Nerve, Arch. Surg. **19**:1577 (Dec., pt. 2) 1929. Hudson, W. A., and Jarre, H. A.: Cin-Ex Camera Studies of the Tracheobronchial Tree, Arch. Surg. **19**:1236 (Dec., pt. 2) 1929. Heinbecker, P.: Caliber Changes in the Bronchi in Normal Respiration, Arch. Surg. **19**:1574 (Dec., pt. 2) 1929. Jackson, C.: The Bronchial Tree: Its Study by Insufflation of Opaque Substances in the Living, Tr. Am. Laryng. A. **40**:319, 1918. Kuntz, A.: The Autonomic Nervous System, Philadelphia, Lea & Febiger, 1929, p. 176.

4. Thornton, W. L., and Pratt, J. P. : The Relation of Bronchial Stenosis to Bronchiectasis, Bull. Johns Hopkins Hosp. **19**:230 (Aug.) 1908.

5. Eloesser, L.: Bronchial Stenosis in Pulmonary Tuberculosis with Some Notes on Tuberculous Stenosis of Trachea and Bronchioles, Am. Rev. Tuberc. **30**:123 (Aug.) 1934.

6. Jackson, C.: (*a*) A New Diagnostic Sign of Foreign Body in Trachea and Bronchi: The Asthmatoid Wheeze, Am. J. M. Sc. **156**:625 (Nov.) 1918; (*b*) Mechanism of Physical Signs in Neoplastic and Other Diseases of Lung with Especial Reference to Atelectasis and Emphysema, J. A. M. A. **95**:639 (Aug. 30) 1930.

7. Schick, Bela: Expiratorisches Keuchen als Symptomatologie in ersten Lebensjahre, Wien. klin. Wchnschr. **23**:153 (Feb. 3) 1910.

marked diminution or absence of breath sounds and depression and immobility of the diaphragm.[8] The asthmatoid wheeze may be heard on auscultation of the chest. Moist râles, due to secretion formed at or behind the obstruction, may be evident. These sounds, while an aid to diagnosis, do not localize the obstruction.[6a]

The roentgenogram shows, on the affected side, a greater penetration of roentgen radiation (i. e., the affected side will be darker), increased width of the intercostal spaces, deviation of the heart and trachea to the other side and a depression and flattening of the diaphragm. These changes are less apparent when the roentgenogram is made during inspiration and are exaggerated if the exposure occurs during expiration.[9]

Fluoroscopic examination shows the changes noted on the roentgenogram and the limitation of movement of the diaphragm on the affected side, with little or no movement of the ribs.[10]

It is difficult to state the actual incidence of tuberculous lesions causing bronchial obstruction leading to emphysema. There are many reports of obstruction to the trachea,[11] such as rupture of glands into the bronchi or trachea with fatal asphyxiation [12] or sloughing of a gland into the respiratory passages with asphyxial death later owing to impaction at the larynx.[13] A reasonably complete search of the literature has yielded a relatively small number of cases of partial obstruction with emphysema due to tuberculous glands. Those who have reported cases frequently have mentioned two or three personal observations.

8. Riegel, F., in von Ziemssen, H.: Cyclopedia of the Practice of Medicine, New York, William Wood & Company, 1876, vol. 14, p. 275. Brünings, W.: Diagnose und Behandlung der in den Luftwegen befindlichen Fremdkörper, Deutsche med. Wchnschr. **38**:929 (May 16) 1912. Lord, F. T.: Certain Aspects of Diagnosis of Bronchostenosis, J. Thoracic Surg. **1**:573 (Aug.) 1932.

9. Iglauer, S.: Tracheobronchoscopy with Report of Cases, Ohio State M. J. **7**:178 (April) 1911.

10. Manges, W. F.: Roentgen-Ray Diagnosis of Non-Opaque Foreign Bodies in Air Passages, Am. J. Roentgenol. **9**:288 (May) 1922. Manges, W. F.; Jackson, C., and Spencer, W. H.: Diagnosis and Localization of Non-Opaque Foreign Bodies in Bronchi, ibid. **7**:277 (June) 1920.

11. (*a*) Scobie, R. B.: Acute Asphyxia from Intrabronchial Rupture of Tuberculous Mediastinal Gland with Recovery, Am. J. Dis. Child. **48**:373 (Aug.) 1934. (*b*) Bilderback, J. B., and Ashley, C. G.: Tracheobronchial Obstruction Produced by Tuberculous Lymphadenitis, J. Pediat. **6**:199 (Feb.) 1935.

12. Scobie.[11a] Löhrer: Ein Fall von vollkommener Ausstopfung der Trachea durch verkäste und gelöste Bronchial-lymphknoten nach Perforation in den Anfangsteil des rechten Bronchus, München. med. Wchnschr. **51**:1205 (July 5) 1904. Eckert, D.: Zur Frage der expiratorischen Dyspnoea bei Bronchialdrüsentuberculose der ersten Lebensjahre, Charité-An. **34**:266, 1910.

13. Loeb, M.: Durchbruch einer käsigentarteten Bronchialdrüse in den rechten Bronchus, Jahrb. f. Kinderh. **24**:353, 1886. Voelcker, A.: Ulceration of a Caseous Bronchial Gland into the Bronchus: Fatal Asphyxia, Tr. Path. Soc. Lond. **49**:22, 1897-1898.

This might lead one to the assumption that the condition is relatively common but not frequently reported. Eighteen typical cases were found with sufficient data given to warrant their inclusion and evaluation in this series. Two were atypical in that there was atelectasis of one lobe combined with emphysema on the same side. One case was not considered typical on physical or roentgen examination, but on postmortem examination a partial obstruction of a bronchus was found.

The earliest report was that published by Bird [14] in 1842-1843. His patient, a girl aged 18 years, with a history of tuberculosis in the family, had diminished breath sounds on the left side, associated with "sonorous percussion." The patient died. Postmortem examination disclosed that the left lung was emphysematous owing to a partial obstruction of the left main bronchus, which had been compressed between two tuberculous glands.

The list of reported cases is given in the table:

Data on the Cases Reported in the Literature of Obstructive Pulmonary Emphysema Due to Partial Obstruction of the Bronchi by Tuberculous Lesions *

Authors	Cases	
	Typical	Atypical
Bird [14]	1	..
Kohn: Am. Rev. Tuberc. **17**: 565 (June) 1928	..	1†
Wallgren: Acta paediat. **4**: 286, 1925; Acta radiol. **7**: 595, 1926	2	1†
Odelberg-Johnson: Acta radiol. **7**: 229, 1926	..	1‡
Peshkin and Fineman: J. A. M. A. **86**: 1429 (May 8) 1926	3	
Myerson: Arch. Otolaryng. **12**: 627 (Nov.) 1930	2	
Huizinga: Nederl. maandschr. v. geneesk. **17**: 189, 1930; Acta oto-laryng. **16**: 141, 1931	2	
Stone: South. M. J. **24**: 350 (April) 1931	1	
Hart: South. Med. & Surg. **95**: 11 (Jan.) 1933	1	
Eliasberg: Jahrb. f. Kinderh. **139**: 12, 1933	2	
Orel: Jahrb. f. Kinderh. **139**: 379, 1933	1	

* In the chapter on tuberculosis by Sauer in Abt's "Pediatrics" (Abt, Isaac A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1925, 1 ed., vol. 5, p. 342) there is a roentgenogram labeled "Tuberculosis of the Bronchial Glands," which closely resembles the condition described in this case. In a personal communication Dr. Sauer stated that emphysema was present on the right side. The patient might be included in the present series.

† The upper lobe is atelectatic and the lower lobes emphysematous.

‡ The clinical diagnosis was not definite but obstruction was found post mortem.

The following four cases illustrate the symptoms and physical findings that result from partial obstruction of a bronchus by tuberculous lesions of various types.

REPORT OF CASES

CASE 1.—G. G., a 10 month old full term boy weighing 6 pounds and 11 ounces (3,030 Gm.) at birth, was brought to the Children's Memorial Hospital on March 24, 1934, because of rapid breathing. The baby had been well until the age of 5 months. At that time the rapid breathing started and persisted to the time of admission. A nonparoxysmal cough occurred about six or seven times a day. The cough and the rapid breathing had steadily increased in severity, so that just

14. Bird, G.: Fatal Pressure on the Bronchus by Enlarged Bronchial Glands, Lancet **1**:182 (Oct. 29) 1842.

previous to the time of admission the child became cyanotic whenever he cried or coughed. No history of aspiration of a foreign body could be elicited. There was no known exposure to tuberculosis.

Physical examination showed the patient to be a well developed and well nourished baby. When he cried, he became slightly cyanotic. Each wail was cut short by a limited supply of air. The chief departures from the normal were in the chest. There was an easily detectable increase in the anteroposterior diameter of the left side of the chest, with limitation of the respiratory excursion. That side was somewhat resistant to percussion but was distinctly tympanitic. The breath sounds were practically absent on that side. The heart appeared to be on the right side. A foreign body partially obstructing the left main bronchus was at first thought to be the cause of the emphysematous condition.

Roentgen examination revealed that the heart and the mediastinum were displaced markedly to the right, so that in the upper portion of the chest the medias-

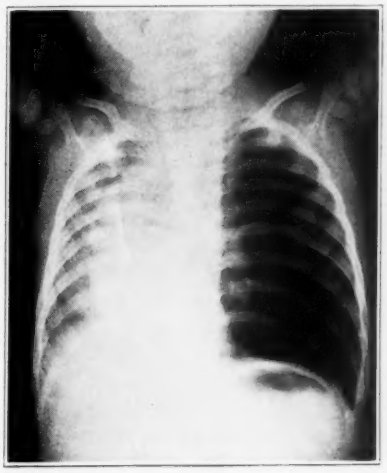

Fig. 1.—Roentgenogram of G. G., 8 months old, with cyanosis and dyspnea of five months' duration and a positive Mantoux reaction. The heart has shifted markedly to the right. The left intercostal spaces are widened, and the left side of the diaphragm is depressed. Increased penetration of roentgen radiation is indicated on the left side. A hilus gland is present on the left side.

tinum came to within 1.5 cm. of the right wall of the chest. The left side of the chest was emphysematous, with the usual findings of widening of the intercostal spaces, depression of the diaphragm and diminished density of the lung (fig. 1). An oval shadow, 2.5 by 4 cm. in diameter, was present in the hilus of the left lung. On fluoroscopic examination, the diaphragm did not move on the affected side.

A Mantoux test with a 1:10,000 dilution of tuberculin gave a markedly positive reaction. On the basis of these findings, the diagnosis was changed to partial obstruction of the left main bronchus due to an encroaching tuberculous gland. A bronchoscopic examination was made by Dr. Thomas C. Galloway, who gave the following report: "The left main bronchus was roughly crescentic in cross-section. The mucosa was intact, with no exudate present. The deformity appeared to be due to an extrabronchial mass pushing in the anterolateral wall of the bronchus." This confirmed the original impression that the obstruction was due

to an enlarged tuberculous gland which appeared in the roentgenogram in the region of the hilus of the left lung.

After four treatments with 122.8 roentgens over the upper part of the mediastinum anteriorly at three day intervals, the child was discharged as improved. The patient did reasonably well at home for one month, but at the end of that period he contracted a cough associated with cyanosis and a marked increase in dyspnea. The child was seen by Dr. Charles Schott and was hospitalized at St. Joseph's Hospital of Chicago. Dr. Schott granted me permission to present the subsequent history and roentgenograms.

At the time of admission to St. Joseph's Hospital the left side of the chest was reported as hyperresonant over the upper portion but somewhat dull over the lower portion posteriorly. The breath tones were absent over the left side. The right side was resonant. The heart deviated to the right. An intermittent fever, the temperature varying from normal to 105 F., was present. A roentgenogram taken of the chest at this time resembled the original pictures but differed in that it

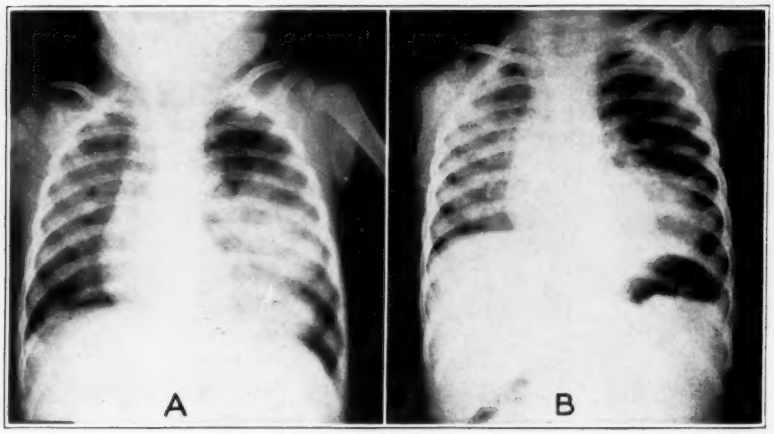

Fig. 2.—Roentgenogram of G. G. at the age of 10 months. *A*, exacerbation of dyspnea and cyanosis and displacement of the heart (less than in figure 1). Note the shadows in the midportion of the left side of the chest and the rough triangular density from the left hilus to the diaphragm. *B* shows the condition four months later. The heart is still displaced. There are increased aeration of the left side of the chest and widened intercostal spaces on the left side. The shadow in the middle of the left side of the chest has disappeared, but the one at the base is still present.

showed that the heart and trachea were not deviated as far to the right. Two new shadows were present in the left side of the chest, one in the midportion and another extending from the hilus to the diaphragm (fig. 2 *A*). These doubtless represented bronchiogenic dissemination of tuberculosis following rupture into the bronchus of the previously observed gland. A roentgenogram taken four months later disclosed a clearing of the shadow in the lower lobe. The evidence of an obstructive emphysema was still present (fig. 2 *B*).

Comment.—This child, at the time of bronchoscopic examination, had a smooth, partially obstructing deformity of the left main bronchus due

to pressure from without, in all probability from a tuberculous hilar gland. It had been present for about five months, if one may assume that this was the cause of the dyspnea. The gland probably broke down and ruptured into the bronchus, accounting for the exacerbation of cyanosis, dyspnea and fever and the disseminated lesion which appeared later. It is probably safe to assume that a mass of tuberculous granulation tissue at the site of the rupture and caseous material in the trachea and bronchus were the cause of the residual obstruction.

Case 2.—M. M., a 3½ year old girl, entered the Children's Memorial Hospital on March 26, 1932, with acute tonsillitis and rhinitis. The fact that the child's father was a patient at a tuberculosis sanatorium prompted further investigation. A Pirquet test gave positive results. A roentgenogram showed a definite mottled and blurred density in the right hilus and an enlarged gland in the right side of

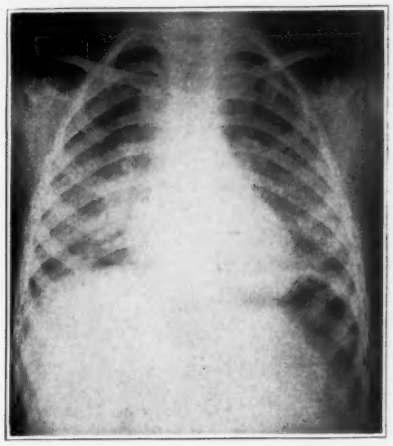

Fig. 3.—Roentgenogram of M. M. at the age of 3½ years, with a positive Pirquet reaction, showing mottled density in the right hilus and smooth round density in the upper part of the mediastinum on the right side.

the mediastinum (fig. 3). Four months later, in July, a tuberculous gland in the neck enlarged, broke down and discharged. This drained for four months and then subsided. The child did poorly, gained weight slowly and had a constant productive cough. A roentgenogram taken in August 1933, one month before the acute disturbance of the respiratory tract to be described, showed some recession of the tuberculous process. There was no evidence of gross obstruction to a bronchus in the roentgenogram taken at that time.

In September 1933 the patient was readmitted for acute pain and swelling in the upper portion of the left side of the chest, which had been preceded by a severe paroxysm of coughing and expectoration of "one-quarter cupful" of frothy sputum. When examined, the child was dyspneic and had an expiratory wheeze and retractions of the suprasternal and infrasternal regions. There was a subcutaneous emphysema of the upper portion of the left side of the chest extending up over the left shoulder and the left side of the neck. The breath sounds were suppressed

over the right side. Because of the child's acute distress, further accurate examination could not be made at the time.

Both subcutaneous and mediastinal emphysema were clearly defined on the roentgenogram (fig. 4 *A*). In addition, the roentgenogram showed hyperaeration of the right lung, widening of the right intercostal spaces, depression of the right side of the diaphragm and displacement of the heart to the left. The subcutaneous emphysema cleared up in about five days (fig. 4 *B*). As this receded the hyperresonance of the right side, the larger right hemithorax and the suppression of breath sounds became more evident. The heart seemed displaced to the left, but this could not be definitely established. Attacks of acute dyspnea, with retraction of the suprasternal and infrasternal regions, cyanosis and asthmatoid wheezing, occurred at frequent intervals associated with large moist râles over the left lung. By October 28 the results of both physical and roentgen examination were normal, with a cessation of the dyspneic attacks (fig. 5 *A*).

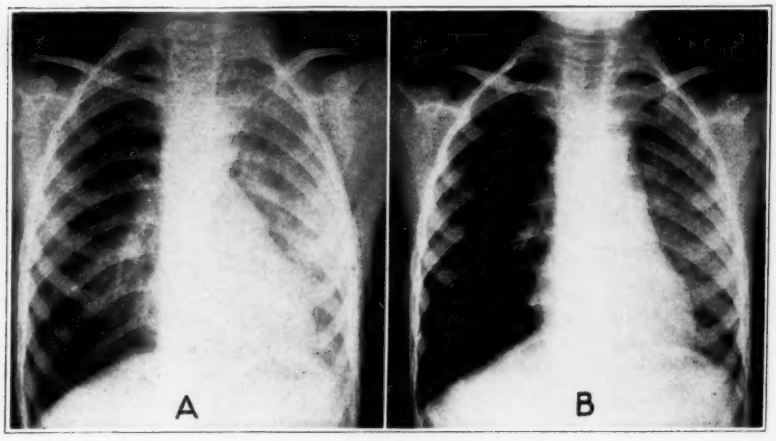

Fig. 4.—*A*, roentgenogram of M. M. taken eighteen months after the view shown in figure 3, and immediately after rupture of a gland into the right main bronchus. Note the subcutaneous emphysema in the left axillary region. The heart is displaced to the left. The right side of the chest shows the changes induced by hyperaeration. *B*, roentgenogram showing the chest six days later after the subcutaneous emphysema has disappeared.

Bronchoscopic examination was deferred until March 1934, six months later. At that time there were no physical or roentgen signs of bronchial obstruction (fig. 5 *B*). Dr. Thomas C. Galloway made a bronchoscopic examination while the patient was under avertin narcosis. He reported, "Granulation tissue, ulcerative in character and somewhat fungating was present in the right main bronchus." The child's condition was too poor to permit extended study or biopsy.

Comment.—In this instance the persistent morning cough was probably due to irritation of the bronchial mucosa by a hilar gland.[7] There was no opportunity to examine the child during this period, but the roentgenogram showed no evidence of bronchial obstruction severe enough to produce an emphysema. That the rupture of a gland into the

right main bronchus did occur is supported by the sudden onset of a severe coughing spell, more violent and productive than usual, and by the break in continuity of the bronchus leading to the mediastinal and subcutaneous emphysema. The obstructive emphysema cleared rapidly. No gross spread of bronchiogenic tuberculosis could be detected. The history resembles that in a case reported by Paunz.[15]

Case 3.—L. B., a Negro boy, was referred by the Northwestern University Clinic to the Children's Memorial Hospital in April 1931 at the age of 3 years and 3 months. He had been well until eight weeks before admission, when he became feverish and listless. An uncle, who had died one year previously of tuberculosis, had visited the family occasionally. A sister, aged 14, had tuberculosis and was a patient at the Cook County Hospital.

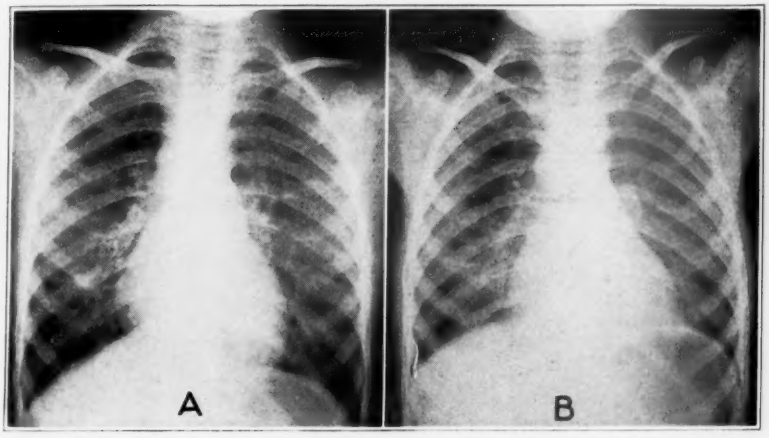

Fig. 5.—*A*, roentgenogram of M. M. taken forty days after rupture of the gland into the right main bronchus, showing restoration of normal aeration. *B*, roentgenogram showing normal aeration six months after the accident. At this time, bronchoscopic examination showed granulation tissue present in the right main bronchus.

On physical examination, suppression of breath sounds and relative dulness, confined to the upper portion of the right side of the chest anteriorly, were found.

Roentgen examination of the chest visualized a widening of the mediastinum in the region of the fourth rib and circular density in the inner third of the right lung (fig. 6*A*). The child stayed one week at the hospital, during which time the temperature was normal, and he was discharged with a diagnosis of tuberculosis of the hilar glands.

He was not seen again until Jan. 30, 1933. He had had a cough of six months' duration, which had become more severe and productive in the preceding two months. His appetite was good, but he had gained only 3 pounds (1.3 Kg.) from 1931 to 1933. The sister, meanwhile, had died of tuberculosis.

15. Paunz, M.: Beitrag zur Diagnose des Durchbruchs tuberkulöser Tracheobronchialdrüsen in die Luftwege, Ztschr. f. Hals-, Nasen- u. Ohrenh. **32**:599, 1933.

Examination of the chest revealed hyperresonance of the right side with markedly suppressed breath sounds. The heart had shifted to the left. Roentgenograms showed increased roentgen penetration, widening of the interspaces and depression and flattening of the diaphragm on the right. A horizontal wedge-shaped shadow at the level of the transverse interlobar fissure, with additional haziness of the mesial half of the right lung field, was present. No tubercle bacilli were recovered from gastric lavage. After discharge, he was seen twice in the outpatient department, where it was noted that an expiratory wheeze and an increase in the anteroposterior diameter of the right side of the chest had developed. Roentgenograms at that time showed an increased scarring in the region previously pointed out as cloudy (fig. 6 *B*).

The child was reexamined in December 1934, approximately two years later; the findings, both physical and roentgenologic, were practically unchanged.

Comment.—This child presented another type of bronchial obstruction, that is, one which had persisted for two years. It is impossible

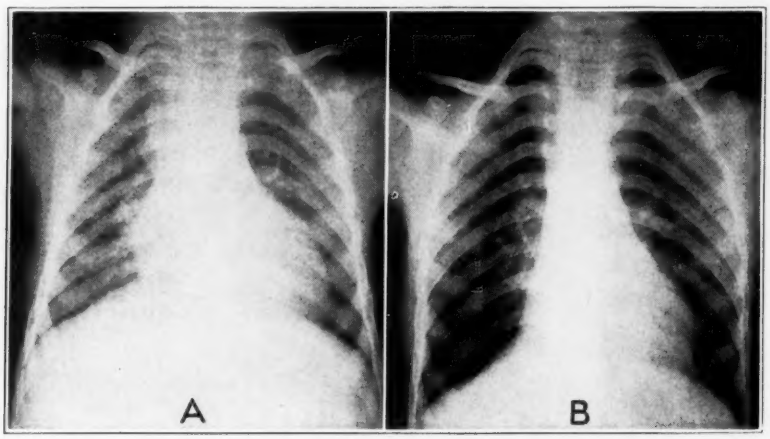

Fig. 6.—*A*, roentgenogram of L. B. at the age of 3 years and 3 months, showing a tuberculous gland in the mediastinum on the right side. *B*, roentgenogram taken at the age of 6 years. The heart has deviated to the left, and the interspaces are widened on the right. The diaphragm is depressed on the right, and increased penetration of roentgen radiation is indicated on the right (these changes show up more clearly on the original plates).

to state with any certainty either the mode or the time of onset of this condition. No indication of any respiratory accident could be found in the history, though this does not exclude its occurrence.

The obstruction was, apparently, either a stenosis on an entirely different basis from those of the first two patients or a later stage of the same condition. Either would probably be the result of the contraction of scar tissue. Complete contraction would, of course, result in atelectasis of the affected lung.[16]

16. Eloesser, L.: Bronchial Stenosis, J. Thoracic Surg. **1**:485 (June) 1932.

With the permission of Dr. Clifford G. Grulee and Dr. Eleanor I. Leslie, the following case, with the results of bronchoscopic and postmortem examinations, is presented. They furnished the complete history, roentgenograms, protocols of the autopsy and an accurate drawing of the pathologic processes found after death.

Case 4.—R. H., a full term 7½ month old boy weighing 5 pounds and 15 ounces (2,890 Gm.) at birth, was admitted to the service of Dr. Grulee and Dr. Leslie at the St. Francis Hospital in Evanston on Aug. 1, 1931, for "difficulty in breathing as if a whistle were in his throat."

The patient contracted a cough when 4 months of age, and at that time the difficulty in breathing, associated with "whistling," made its appearance. During the cold weather the condition was aggravated, and during the warm weather it appeared to subside. Most of the time the breathing was shallow, heavy and fast. During the week before admission he lost 10 ounces (280 Gm.). Fever was noted for five days before hospitalization. There was no known exposure to tuberculosis.

On examination, the child appeared irritable and seemed to be having extreme difficulty in breathing. Over the left side of the chest no breath sounds were heard. The percussion note was described as ranging from flat to dull. The right side was normal. The remainder of the examination gave no noteworthy results.

The tentative diagnosis was tuberculous lymph nodes causing pressure on the left main bronchus.

A roentgenogram revealed the heart shifted to the right, that is, away from the side of absence of breath tones; increased penetration of roentgen radiation, depression of the diaphragm and wide separation of the ribs on the left side. At the left hilus and extending upward there was an oval density, 1.5 by 4 cm. in extent (fig. 7).

The difficulty in breathing persisted, and on August 11, ten days after admission, a bronchoscopic examination was made by Dr. Lewis F. McBride. A complete closure of the left bronchus due to extrabronchial pressure was reported.

On August 13 roentgen therapy was resorted to in an attempt to reduce the size of the obstructing gland. This was ineffectual. The breathing became so labored that a tracheotomy was performed to alleviate the obstruction. This only partially relieved the dyspnea.

On August 21, roentgen therapy was again administered to the peribronchial glands. Four days later a roentgenogram showed a return of the mediastinum to normal and equal penetration of the radiation on both sides. This, associated with audible breath sounds on the left side, confirmed the impression that the obstruction was relieved.

On August 27, the child had a convulsion. Two days later, rigidity of the limbs, staring eyes, a Kernig sign, ankle clonus and a spinal fluid cell count of 250 prompted the diagnosis of a tuberculous meningitis. A Pirquet test gave positive results. The child gradually failed, had periods of marked dyspnea and died on Sept. 15, 1931.

The autopsy was reported by Dr. O. T. Schultz, pathologist at the St. Francis Hospital:

The anatomic diagnosis was: caseous tuberculosis of the lower lobe of the left lung, with cavity formation; caseous tuberculosis of the peribronchial lymph nodes; miliary tuberculosis and lobular tuberculous pneumonia of both lungs:

caseous tuberculosis of the mesenteric lymph nodes; ulcerative tuberculosis of the lower part of the ileum and appendix; tuberculous meningitis.

The surface of the anterior portion of the lower lobe of the left lung was grayish. This part of the lung was consolidated and airless. The central portion of the area felt somewhat softer than the rest. The pleura of this area was united to that of the upper lobe by fine fibrous adhesions. The posterior portion of the lower lobe contained air and was deeply congested. The upper lobe was pale and crepitant. Beneath the pleura of the upper lobe could be felt and seen numerous minute gray, translucent nodules, from 1 to 2 mm. in diameter. On section, the airless portion of the lower lobe measured 4 by 5 cm. in the long axis of the lung and 2 cm. in the transverse axis. The cut surface was yellowish gray, opaque and airless and had a finely lobulated appearance. At the center of the area was an irregular cavity with a ragged wall and no limiting membrane, 2 cm. in diameter. In the lower lobe, superior to this area, were a number of opaque yellowish areas formed by the fusion of groups of nodules. The cut surface of the upper lobe was studded with many small translucent nodules like those seen beneath the pleura and by an even larger number of slightly larger gray, translucent areas of lobular size and distribution. Above the main bronchus of the left lung was a group of enlarged and fused lymph nodes, the mass being 1.3 cm. in diameter. Below the bronchus opposite the mass was an enlarged node 1.7 cm. in diameter. Anterior to the bifurcation of the trachea, more to the left than the right and more closely related to the left main bronchus than the right, was a mass of enlarged nodes 2 cm. in diameter. Embedded in the tissue of the root of the lung about the bronchus were several nodes from 5 to 7 mm. in diameter. All of these nodes on section were opaque, yellowish gray and caseous. The situation of the larger nodes about the root of the left main bronchus was such as to have caused compression of this bronchus (fig. 8). There had been apparently some narrowing of the terminal portion of the trachea by the mass lying anterior to the bifurcation. The lower lobe of the right lung was congested. Beneath the pleura of the upper and middle lobes, which were pale, could be

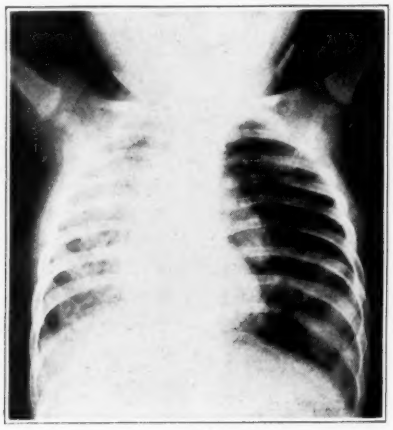

Fig. 7.—Roentgenogram of R. H. at the age of 7½ months, with a positive Pirquet reaction, showing the mediastinum shifted to the right and the density in the left hilus.

seen many miliary nodules like those of the left lung. On section, the cut surface of these lobes revealed the same miliary and lobular involvement as the upper lobe of the left lung. Only a few tubercles were seen on the cut surface of the lower lobe. At the hilus of the lung were several caseous nodes from 4 to 7 mm. in diameter. A macroscopic area of rupture of a caseous node into the vessels of the lung could not be detected.

The stomach and intestines were collapsed and contained little material. At the lower end of the ileum, for a distance of 4 cm. upward from the ileocecal valve, the mucosa was elevated, finely nodular and pale. In this area, which involved the entire circumference of the ileum, were a number of areas of ulceration from 2 to 4 mm. in diameter. The margins of the ulcers were irregular and only

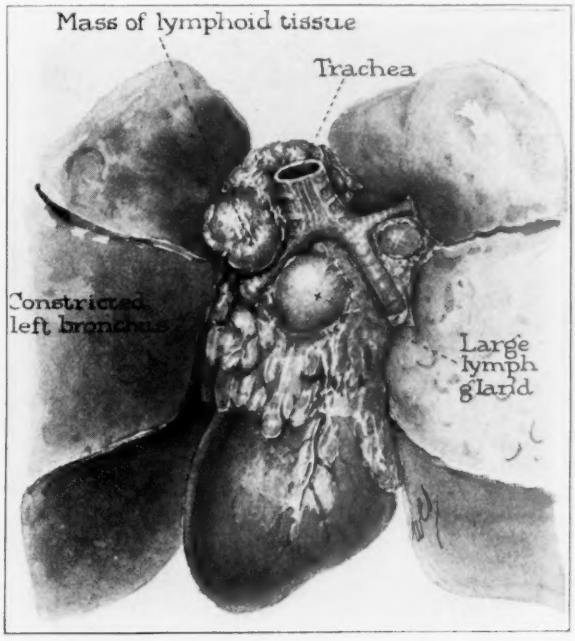

Fig. 8 (case 4).—Drawing (posterior view) showing the compression of the left main bronchus by enlarged tuberculous glands.

slightly congested. A Peyer patch above the area described was 2 cm. long, swollen, raised and pale, and it contained a small central area of ulceration. The mucosa of the appendix had a finely nodular appearance owing to swelling of the lymphoid follicles. At the center of seven of these nodular enlargements was a small, punched-out ulcer. The diameter of these ulcers was from 1 to 2 mm. All of the mesenteric lymph nodes were enlarged, those of the ileocecal region being enlarged to the greatest extent. The larger nodes here and throughout the mesentery on section were gray, opaque and caseous.

An increased amount of clear liquid was present beneath the brain. The vessels of the convex surface were congested. The opposed mesial surfaces of the frontal lobes were united to each other by fine fibrous adhesions. An increased amount of fluid was present beneath the pia. The fluid was slightly cloudy. The pia of

the base of the brain was slightly thickened, the thickening extending upward laterally in the sylvian fissure. In the thickened meninges could be seen very many small, translucent tubercles. On section, the lateral ventricles were not dilated, and the brain tissue appeared normal. The base of the skull was normal. The left middle ear was opened; it appeared normal.

Comment.—This patient presented the complete syndrome, with the typical history of dyspnea, cyanosis and wheezing, the characteristic physical and roentgen findings, the bronchoscopic proof of obstruction and, finally, the demonstration of the tuberculous gland at autopsy.

GENERAL COMMENT

Critical review of the history and of the results of physical and roentgen examination of these four patients serves to separate their conditions rather than to group them under the same heading. All show the phenomenon of obstructive emphysema induced by tuberculosis, but they differ in mechanism of induction. In the first patient, G. G., the obstruction was present for six months before the softened gland ruptured into the bronchus. Here a gross spread of bronchiogenic tuberculosis occurred. In the roentgenograms made after this accident, the shadow in the midportion of the chest may represent complete obstruction either by caseous material or granulation tissue, since subsequent pictures showed a clearing, or it may represent an area of pneumonia which subsided. Granulation tissue projecting into the left main bronchus, an external deforming gland or scar tissue may be responsible for the persistence of the obstruction.

In the second patient, the entire course was condensed into a short period of time, the obstruction being present only during the period of rupture and discharge of the caseous content of a gland. The granulation tissue present in the bronchus six months later was not sufficiently extensive to embarrass the flow of air through the bronchus. It is speculative to predict what deformity, if any, will occur when the lesion heals. It is not beyond reason to assume that contracture of the bronchus may ensue. If this is complete, atelectasis will occur; if it is incomplete, a persistent emphysema will result.

The third patient, with emphysema of two years' standing, probably presented the same condition in a chronic phase, arrived at by contracture of scar tissue after healing had occurred.

The fourth patient resembled the first in having a partial obstruction from without by pressure from a tuberculous gland. Death was due to a terminal tuberculous meningitis rather than the more usual asphyxiation.

SUMMARY

Incomplete obstruction of a main bronchus of tuberculous origin will result in emphysema of the lung on that side if the lesion is suffi-

ciently large. The physical and roentgen findings are characteristic and complementary. The obstruction may be acute or chronic; it may be induced by a gland's eroding the wall of a bronchus and projecting into its lumen, by rupture of a softened gland into a bronchus, by granulation forming at the site of such rupture or by later contracture of the scar of the original lesion. Four cases are reported which illustrate these conditions, with the observations at autopsy in one.

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CHOLESTEROL OF THE BLOOD PLASMA IN THE NEONATAL PERIOD

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The investigation described in this paper[1] represents part of a comprehensive study of the cholesterol in the blood of normal and diseased human subjects. Although the field has been studied extensively by many workers in the past, I felt justified in undertaking such a study for the following reasons:

1. There are wide differences in the normal values for total cholesterol of the serum reported by different authors, the range between minimum and maximum average values amounting to almost 100 per cent of the minimum.[2] The inconsistent results are due, in considerable part, to the use of inaccurate methods. The frequent publication of new procedures for the determination of cholesterol indicates that none has been found to be entirely satisfactory. Recently Schoenheimer and I[3] described a method which permits the rapid determination of total and free cholesterol with satisfactory accuracy in 0.2 cc. of serum or plasma.[4] The availability of the procedure made the present study possible.

2. Many investigations have been concerned with the determination of cholesterol in whole blood. Such studies are of relatively little value since the cholesterol of the red cells and that of the serum have no evident relation to each other. The cholesterol of the red cells is present entirely as free cholesterol in relatively constant amount, while the cholesterol of the serum is largely combined with fatty acids and varies within wide limits. Analysis of whole blood is comparable to the determination of cholesterol in a mixture of approximately equal parts of two different tissues, such as liver and adrenal gland.

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1. This investigation was made possible by the aid of the Josiah Macy Jr. Foundation.

2. Bürger, M.: Der Cholesterinhaushalt beim Menschen, Ergeben. d. inn. Med. u. Kinderh. **34**:624, 1928.

3. Schoenheimer, R., and Sperry, W. M.: A Micromethod for the Determination of Free and Combined Cholesterol, J. Biol. Chem. **106**:745, 1934.

4. Serum and heparinized plasma contain the same amounts of cholesterol, but oxalated plasma contains significantly smaller amounts (Sperry, W. M., and Schoenheimer, R.: A Comparison of Serum, Heparinized Plasma, and Oxalated Plasma in Regard to Cholesterol Content, J. Biol. Chem. **110**:655, 1935).

3. In most investigations only the total cholesterol has been determined, relatively few analyses of free and combined (esterified) cholesterol having been reported. I am convinced that the determination of these fractions is of far greater value in establishing variations from normal than the simple measurement of total cholesterol. Most authors have found that healthy persons differ widely in the amount of total cholesterol in the serum. For example, in our own experience,[5] Dr. Schoenheimer and I found that eighty-seven young adults in good physical condition showed values ranging from approximately 130 to 350 mg. per hundred cubic centimeters. Obviously, unless the total cholesterol content of the serum of a patient is extremely low or high, one cannot be certain that the amount found is abnormal for that person. In contrast, the ratio of combined to free cholesterol is relatively constant. In the same series of eighty-seven subjects, despite a variation of approximately 170 per cent in the values for total cholesterol, the minimum ratio of combined to free cholesterol was 2.31 and the maximum ratio was 3.12,[6] which is to say that the proportion of total cholesterol present in the form of combined cholesterol varied between approximately 70 and 75 per cent only. In disease distinct deviation from the normal ratio may occur. For example, it was pointed out first by Thannhauser and Schaber [7] and confirmed by Epstein [8] that the ratio of combined to free cholesterol may be reduced markedly, even to zero, in the serum from patients with disease of the liver. Nothing is known about the cause of such variations, and there is little information concerning the conditions under which they occur.

Although several workers have studied the total cholesterol content of blood serum and plasma in infants and children, no one appears to have determined the relative amounts of free and combined cholesterol. The primary purpose of the present investigation was to supply such data for normal infants in the neonatal period. In addition, some new information concerning total cholesterol was obtained.

EXPERIMENTAL METHOD

The concentration of total and free cholesterol was determined by the method of Schoenheimer and Sperry [3] in ninety-seven samples of heparinized blood plasma

5. Sperry, W. M., and Schoenheimer, R.: Unpublished results.

6. The actual range may be even smaller than these results indicate, since in the calculation of the ratio the error of the determination of total cholesterol enters once (in the calculation of combined cholesterol) and the error of determination of free cholesterol enters twice. The probable error of the ratio is, therefore, relatively high.

7. Thannhauser, S. J., and Schaber, H.: Ueber die Beziehungen des Gleichgewichtes Cholesterin und Cholesterinester im Blut und Serum zur Leberfunktion, Klin. Wchnschr. **5**:252, 1926.

8. Epstein, E. Z.: The Cholesterol Partition of the Blood Plasma in Parenchymatous Diseases of the Liver, Arch. Int. Med. **47**:82 (Jan.) 1931.

from sixty-three infants, from 1 to 25 days old, and in seven samples of blood plasma from the cord. The amount of combined cholesterol was calculated as the difference between the values for total and free cholesterol. The samples of plasma were obtained through the cooperation of Dr. Donovan J. McCune and Dr. Hilde Bruch, who secured the blood in connection with another study. All of the infants were born in the Sloane Hospital for Women and showed no evidence of disease aside from occasional slight dehydration. About one third of the subjects exhibited the so-called physiologic icterus [9] in mild degree between the second and the tenth day of life. Blood was obtained by puncture of the antecubital vein, considerable stasis being employed. The few samples of blood from the cord were obtained in the following manner: Immediately after delivery the cord was clamped at two points about 1 meter apart, and the segment between the clamps was cut out and taken to another room, where blood was obtained from the placental vein by puncture with a large needle. Coagulation was prevented by the use of approximately 1 mg. of heparin per cubic centimeter.

OBSERVATIONS

Total Cholesterol.—The results, shown in chart 1, were as follows:

1. There was a wide variation in the total cholesterol content of the plasma comparable to that observed in normal adults. In infants from 4 to 25 days old the minimum was 71 and the maximum was 190 mg. per hundred cubic centimeters. This is equivalent to a range of 168 per cent of the minimum value. In the series of determinations in adults, which was discussed briefly in the introduction, the range was from approximately 130 to 350 mg. per hundred cubic centimeters, equivalent to 169 per cent of the minimum value.

2. Over half of the total cholesterol values in infants 4 to 25 days old were within the range found in adults, but the limits of the range in these infants were considerably lower than the corresponding limits in adults (71 to 190 as compared with 130 to 350 mg. per hundred cubic centimeters). For infants from 4 to 25 days old (seventy-one observations) the average, with its standard deviation, was 133 ± 25 mg. per hundred cubic centimeters; for adults (one hundred and eighteen observations) the average was 209 ± 50 mg. per hundred cubic centimeters. Other investigators [10] have reported that the total cholesterol value of the serum is lower in infants than in older children.

9. The diagnosis of physiologic icterus was made on the basis of careful visual examination of the skin and the mucous membranes of the eyes and mouth. The blood plasma was not examined for bile pigment.

10. György, P.: Untersuchungen über Lipoide und Lipoidwirkungen bei Kindern, Jahrb. f. Kinderh. **112**:283, 1926. Baylac, J., and Sendrail, M.: Les modifications de la cholestérinémie au cours de la croissance, Bull. et mém. Soc. méd. d. hôp. de Paris **52**:33, 1928. Gordon, M. B., and Cohn, D. J.: Cholesterol and Lipoid Phosphorus in Infancy and in Childhood: Normal Incidence in Cord Blood and During Infancy and Early Childhood, Am. J. Dis. Child. **35**:193 (Feb.) 1928.

3. There was a marked increase in the total cholesterol content of the plasma during the first three or four days of life. This was suggested by a general upward trend of the values with age during the period and was strengthened by the findings in a considerable number of infants on whom two or three analyses were made. Successive determinations on the same infant are connected by lines on the charts. In eighteen cases in which one analysis was done during the first three days of life, the next determination showed a much higher value for total cholesterol. In only two instances was a definite increase not observed. In one of the

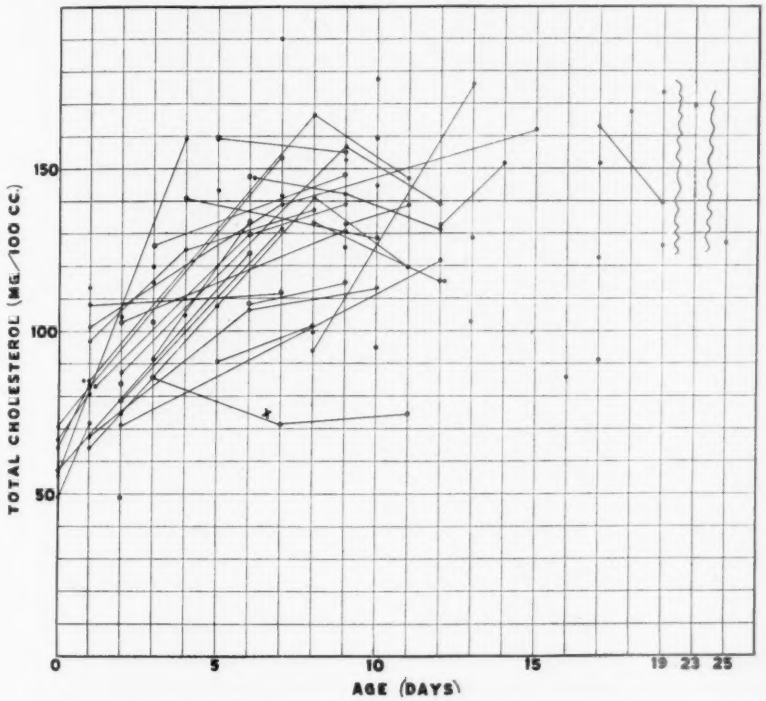

Chart 1.—Variation in the total cholesterol content of the blood plasma with age. Each point or circle represents a single determination. Determinations repeated on the same infant are connected by lines. Circles indicate the presence of physiologic icterus. Determinations at 0 age were made on blood plasma from the cord.

two cases the increase was not significant while in the other (marked "x" on the chart), in which a decrease occurred, there was pronounced icterus which persisted for six weeks after birth. It may be suggested that the increase in the total cholesterol content was associated with dehydration and concentration of the plasma, but in most instances the increases were far too great to be explained by this factor alone. If one omits the two exceptions already noted and the cases in which only

one day separated the first and the second determination, the average increase in fifteen cases was 76 per cent. It is hardly possible that a change of such magnitude could have been due to concentration of the blood plasma, since there was no clinical evidence of severe dehydration in any case. Furthermore, if concentration were responsible, the total protein content should have been increased in proportion to the cholesterol content. When the corresponding values for these two constituents [11] of the plasma were plotted against each other, it was evident that there was no relation between them.

No one appears to have noted such an early and sharp increase in the total cholesterol content as my results demonstrate, though other workers [10] have observed a gradual increase extending throughout childhood. No definite trend is apparent from my data in infants from 4 to 25 days old.

4. No relation between the presence of physiologic icterus and the total cholesterol level could be made out except possibly in the single case, previously mentioned, in which the amount of cholesterol decreased between the third and the seventh day of life to the lowest value recorded in the 4 to 25 day age period.

Ratio of Combined to Free Cholesterol.—Values for the ratio of combined to free cholesterol have not been reported previously for infants and children. The results [12] shown in chart 2 may be summarized as follows:

1. The new-born infants differed from normal adults in two respects: (*a*) The ratio of combined to free cholesterol in most of them was below the minimum ratio (2.3) found in adults, and (*b*) there was a greater range of variation in the infants than in adults (0.7 to 2.6 as compared with 2.3 to 3.1).[6] The difference may be brought out more clearly by expressing the ranges in terms of the percentage of combined cholesterol in the total cholesterol. The equivalent values are from 41 to 72 per cent for infants and from 70 to 75 per cent for adults. The findings indicate that the mechanism, whatever it may be, which controls the proportion of combined and free cholesterol within narrow limits in the adult is not yet fully established in the neonatal period.

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11. The protein analyses were done by Dr. McCune and Dr. Bruch.

12. An unknown number of the first 24 samples analyzed stood at room temperature for extended periods. While this investigation was in progress it was found (Sperry, W. M., and Schoenheimer, R.: Cholesterol Esterase in Blood, J. Biol. Chem. **109**:lxxxvi, 1935) that a marked esterification, with increase in the ratio of combined to free cholesterol, occurs under these conditions. It was necessary, therefore, to omit all of these results, which included all of those on cord plasma, from the chart. All subsequent samples were kept in the icebox, where no change occurs, until they could be analyzed.

2. In the majority of cases in which more than one analysis was made on the same infant, the ratio of combined to free cholesterol increased with advancing age. In all of the infants 14 days of age and older the ratio was over 2; i.e., it was approaching the normal adult level. Unfortunately there are few analyses on the older group and in a number of instances there was a decrease with advancing age; so the conclusion that the ratio of combined to free cholesterol increases during the age period studied is probably not justified on statistical grounds. I merely state that such a tendency is suggested. It will be necessary to extend the studies to older normal infants and children in order to ascertain when the ratio reaches the normal adult range. A few analyses of serum from normal children 1 year of age and older have yielded

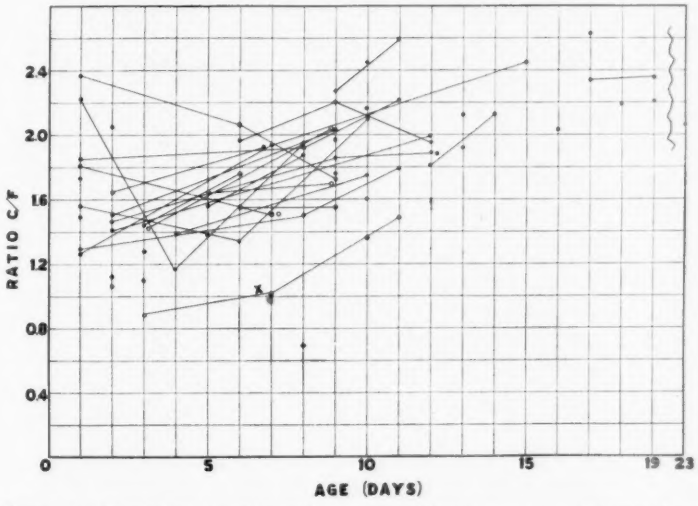

Chart 2.—Variation in the ratio of combined to free cholesterol with age. Each point or circle represents a single determination. Determinations repeated on the same infant are connected by lines. Circles indicate the presence of physiologic icterus.

values similar to those found in adults for both total cholesterol and the ratio of combined to free cholesterol.

3. No effect of physiologic icterus on the ratio of combined to free cholesterol is evident, except possibly in the case marked "x" on the charts, in which unusually low ratios accompanied distinct and persistent jaundice. This is the same case in which a decrease in total cholesterol occurred. On the other hand, the lowest ratio obtained was in an infant 8 days of age with no visible icterus. This lack of any definite relation between the ratio of combined to free cholesterol and the presence of physiologic jaundice is of considerable interest in view of the relation between damage to the liver and decreased ratios of com-

bined to free cholesterol, which has been suggested by previous investigators.[13]

Free and Combined Cholesterol.—These values are not given in detail since they are incorporated in the ratio of combined to free cholesterol which has already been discussed. It may be noted that in infants from 4 to 25 days old (fifty-seven determinations) the minimum amount of free cholesterol found was 25, the maximum 61 and the average 46 mg. per hundred cubic centimeters. For combined cholesterol the values were 36, 126 and 86 mg. per hundred cubic centimeters, respectively.

SUMMARY

The concentration of total and free cholesterol was determined in ninety-seven samples of heparinized blood plasma from sixty-three normal infants during the neonatal period and in seven samples of blood from the cord. The value for combined cholesterol and the ratio of combined to free cholesterol were calculated.

There was a pronounced increase in the total cholesterol content of the plasma in most cases during the first three or four days of life.

The amount of total cholesterol varied within wide limits, with no apparent tendency to increase or decrease, in infants from 4 to 25 days old.

Over half of the total cholesterol values in infants 4 to 25 days old were within the range found in healthy adults, but the limits of the range in these infants were considerably below the corresponding limits in adults.

The ratio of combined to free cholesterol varied widely and in most cases was lower than the minimum ratio found in adults. The regulatory mechanism, which keeps this ratio constant within narrow limits in the adult, is not fully established in the neonatal period.

No definite effect of physiologic icterus either on the ratio of combined to free cholesterol or on the total cholesterol content was evident.

13. Thannhauser and Schaber.[7] Epstein.[8]

BLOOD SUGAR LEVELS AND DEXTROSE TOLERANCE IN EXPERIMENTAL POLIOMYELITIS

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The fact that systemic infection may lead to significant metabolic changes in the host has long been appreciated by clinical observers, who are trained to focus their attention on the whole organism rather than on a given bacteriologic, immunologic or pathologic phase of the disease. In contrast to this, in the study of experimental laboratory infections workers have been so preoccupied with the investigation of specific phenomena of defense, as seen in the altered reactivity of serum and tissue cells, that they have lost sight, as a rule, of the many correlated changes of metabolic nature which assume great significance for a better understanding of the intricate mechanism of the morbid process. Only in recent years, for example, have serious efforts been made to elucidate the nature of diphtheritic intoxication by systematic analysis of disturbances in the carbohydrate metabolism. Among the most important results obtained by a large group of investigators [1] is the discovery that animals given injections of diphtheria toxin show either a marked rise or a pronounced drop in blood sugar content, depending on the severity of the intoxication. It is also generally agreed [2] that such hyperglycemic animals fail to respond to massive doses of insulin. Since there was no need to postulate that the disease lowers the amount of insulin produced by the pancreatic islets or that the toxin destroys the hormone by direct chemical action, Lawrence and Buckley[1a] advanced the hypothe-

This study was made under a grant from the Rockefeller Foundation.

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1 (*a*) Lawrence, R. D., and Buckley, O. B.: Brit. J. Exper. Path. **8**:58, 1927. (*b*) Elkeles, A., and Heimann, F.: Deutsches Arch. f. klin. Med. **155**:263, 1927; **158**:238, 1928. (*c*) Netzley, R. E.: The Effect of Diphtheria Toxin on the Action of Insulin: A Study of the Effect of Infections on Carbohydrate Metabolism in Diabetes Mellitus, Am. J. Dis. Child. **37**:511 (March) 1929. (*d*) Schwentker, F. F., and Noel, W. W.: Bull. Johns Hopkins Hosp. **46**:259, 1930. (*e*) Brems, A.: Klin. Wchnschr. **11**:895, 1932. (*f*) Begg, N. D.: Lancet **1**:480, 1935. (*g*) Mikami, S.: Tohoku J. Exper. Med. **6**:299, 1925. (*h*) Yannet, H., and Darrow, D. C.: J. Clin. Investigation **12**:767 and 779, 1933. (*i*) Rosenthal, F.: Arch. f. exper. Path. u. Pharmakol. **75**:99, 1914.

2. Sweeney, J. S.: Effect of Toxemia on Tolerance for Dextrose and on the Action of Insulin, Arch. Int. Med. **41**:420 (March) 1928.

sis that the observed phenomena are due to overstimulation of the adrenal and thyroid glands, which are said to be physiologically antagonistic to the action of insulin. This theory received direct support in the observation of striking pathologic changes in the thyroid and adrenal glands, and it has been confirmed by subsequent clinical and experimental observations. Yannet and Darrow,[1h] on the other hand, who stressed the significance of hepatic necroses, stated the belief that the varying degrees of hyperglycemia and hypoglycemia are related to changes in the glycogen-forming or glycogen-storing ability of the liver. In cases of diphtheria in human subjects the postmortem examinations made by Elkeles and Heimann [1b] showed pathologic changes not only in the adrenals but in the middle lobe of the pituitary gland as well, substantiating earlier observations [3] and at the same time advancing further evidence for an involvement of the whole endocrine system in the deranged carbohydrate metabolism typical of this disease. More light has been thrown on the nature of this disturbance by numerous studies of dextrose intolerance, both in human beings and in experimental animals with diphtheria, all of which have demonstrated a marked inability on the part of the body to assimilate small amounts of dextrose injected into the circulatory system.[4] This dysfunction characteristically increased with the progress of the toxemia. Most recently, Begg [1f] found the degree of variation in the blood sugar level to be a sensitive index of the severity of the disease, noting, as others had done before, that the administration of insulin would not change the character of abnormal tolerance curves.

In poliomyelitis, metabolic changes have received scant attention. The available data point to an increase in the amount of sugar in the spinal fluid during paralysis or the preparalytic stage.[5] So regular is this phenomenon that it serves as a material aid in establishing the differential diagnosis of the disease in human beings. Our interest in the study

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4. Rosenthal.[1i] Lawrence and Buckley.[1a] Elkeles and Heimann.[1b] Netzley.[1c] Schwentker and Noel.[1d] Brems.[1e] Yannet and Darrow.[1h] Sweeney.[2] Sweeney, J. S., and Lackey, R. W.: The Effect of Toxemia on Tolerance for Dextrose, Arch. Int. Med. **41**:257 (Feb.) 1928. Tisdall, F. F.; Drake, T. S. H., and Brown, A.: The Production of a Lowered Carbohydrate Tolerance in Dogs, Am. J. Dis. Child. **32**:854 (Dec.) 1926. Hector, F. J.: Lancet **2**:642, 1926. Projachka, M.: Bull. et mém. Soc. méd. d. hôp. de Paris **54**:865, 1930. Benn, E. C.; Hughes, E., and Alstead, S.: Lancet **1**:281, 1932.

5. Poliomyelitis, Monograph of the Committee for the Study of Infantile Paralysis, Baltimore, Williams & Wilkins Company, 1932.

of carbohydrate metabolism in experimental poliomyelitis was stimulated by reasoning along two lines. We have repeatedly expressed our conviction that the natural occurrence of poliomyelitic infection is in some way connected with and probably conditioned by an abnormal function of the endocrine system of the host, particularly of the pituitary and adrenal glands.[6] It seemed logical, therefore, to attempt to broaden the basis of this concept by choosing the carbohydrate metabolism as the test object. A second consideration, intimately linked with the first, has come from certain clinical and experimental observations which have demonstrated that diphtheritic intoxication and poliomyelitic infection share some fundamental pathologic features, such as the occurrence of marked cellular changes in the adrenal glands [7] and the disappearance of vitamin C from this tissue during the course of the disease.[8] In addition, we have been able to show that there is a marked parallelism in the ability of various biologic substances, such as antitoxic serum,[9] the medullary and cortical hormone of the adrenal glands [10] and vitamin C,[11] to inactivate both diphtheria toxin and poliomyelitis virus in vitro. The extensive data which have been brought together on abnormalities of carbohydrate metabolism in diphtheria may therefore serve as convenient collateral material to compare with whatever findings were observed in similar studies in poliomyelitis.

EXPERIMENTAL METHOD

In order to collect all pertinent information on the problem under investigation, the experimental work was planned to include: (1) determinations of the blood sugar level in rhesus monkeys suffering from poliomyelitic paralysis; (2) tolerance tests to examine the functional ability of paralyzed monkeys to assimilate a small dose of dextrose injected into the circulation, and (3) tests to determine the effect of insulin on the prevailing blood sugar level in monkeys which were in various states of paralysis. The animals were infected by intracerebral injection of multiple infectious doses of a 10 per cent suspension of the Aycock strain of poliomyelitis passage virus, which has been used in this

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7. Landon, J. F., and Smith, L. W.: Poliomyelitis, New York, The Macmillan Company, 1934.

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9. Jungeblut, C. W.: J. Immunol. **27**:17, 1934.

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11. Jungeblut and Zwemer.[8] Jungeblut, C. W.: J. Exper. Med. **62**:517, 1935.

laboratory with uniform success for a period of over six years. Samples of blood were drawn by puncture of the heart after the animal had been subjected to a period of fasting of from fifteen to eighteen hours. Whenever dextrose was used, the solution was injected into a superficial vein of the leg. Analysis of the blood sugar was carried out with the macroscopic method of Folin and Wu, the values being expressed in terms of milligrams of sugar per hundred cubic centimeters of blood. This method allows for a technical error of ± 10 per cent. Since we were concerned only with the demonstration of gross differences between normal and poliomyelitic animals, it was deemed sufficiently accurate for our purpose.

The experiments which fall under the different headings are described in three separate sections of this paper.

Blood Sugar Levels in Poliomyelitic Monkeys.—For purpose of comparison it became necessary to determine first the physiologic range of values for blood sugar in normal monkeys. Hence, twenty-five determinations were made on a total number of twenty-three normal monkeys. These showed a normal range of from 67.6 to 130.3, the values for nineteen of the twenty-five samples falling between the two extremes of 80 and 120. The average mean for all samples was 97.5. In view of these findings, values for blood sugar in rhesus monkeys which lie between 75 and 125 must be considered as being within the range of normal fluctuations.

We now proceeded to carry out determinations of the blood sugar on monkeys suffering from various degrees of poliomyelitic paralysis, including thirteen with very slight paralysis, nineteen with severe paralysis and fourteen that were prostrated by complete paralysis. As a rule, the same animal was bled repeatedly over a period of several days to compare the blood sugar values with the progress of paralysis. One hundred and twenty-two samples were examined from thirty-eight poliomyelitic monkeys. The range in these tests was from 54.5 to 187, the majority of values, i. e., for eighty-seven samples of the one hundred and twenty-two, lying between 75 and 125. The average mean value was 85.6.

These figures, without further statistical refinement, fail to indicate any significant difference between the blood sugar level of normal monkeys and that of poliomyelitic monkeys. However, in subjecting our material to further analysis, it was found that the eight abnormally high values, i. e., those between 187 and 142, occurred in completely paralyzed animals. While this finding may look significant, it must be remembered that the remaining fifty-eight samples obtained from completely paralyzed monkeys all gave figures within the normal limits. For this reason we are inclined to regard this grouping as being due to chance. Again, if one attempts to classify the results according to the duration of paralysis which extended from one day to ten days and over, no general relationship can be made out between the length of the disease and maximum and minimum blood sugar levels, except that in seven animals there occurred a gradual and progressive increase in the blood sugar shortly before death.

We therefore conclude from these data that the average blood sugar level in poliomyelitic monkeys is not signifiantly different from that observed in normal monkeys and, furthermore, that there is no consistent relation between the height of the blood sugar level and either the extent or the duration of paralysis. However, there may be an antemortem rise of the blood sugar level in some animals.

Dextrose Tolerance Tests in Poliomyelitic Monkeys.—Having failed to discover any clearcut deviation from the normal blood sugar level in various stages of the infection, we next turned our attention to tolerance tests designed to

determine the functional ability of poliomyelitic monkeys to assimilate a given dose of dextrose injected into the circulatory system. These tests were carried out by administering 5 Gm. of dextrose, i. e., 20 cc. of a 25 per cent solution, intravenously after the fasting level had been determined and by making determinations of blood sugar at the end of one-half, one and two hours after the injection of dextrose.

TABLE 1.—*Results of Dextrose Tolerance Tests in Eight Normal Monkeys* *

Number	Blood Sugar Level During Fasting	Blood Sugar Level		
		One-Half Hour After Injection of Dextrose	One Hour After Injection of Dextrose	Two Hours After Injection of Dextrose
O76	98.0	441.0	125.0	69.8
O78	89.3	174.4	55.8	68.2
O79	88.8	333.2	102.0	51.4
O80	130.3	252.0	67.6	63.0
Q7	112.4	224.8	78.4	109.9
Q5	99.0	312.4	83.3	84.0
Q2	105.3	190.4	54.8	69.2
Q6	84.4	300.8	140.8	50.2

* The determinations were made according to the macroscopic method of Folin and Wu after intravenous injection of 5 Gm. of dextrose (20 cc. of a 25 per cent solution).

TABLE 2.—*Results of Dextrose Tolerance Tests in Nineteen Poliomyelitic Monkeys in Various Stages of Paralysis* *

Number	Degree of Paralysis†	Blood Sugar Level During Fasting	Blood Sugar Level		
			One-Half Hour After Injection of Dextrose	One Hour After Injection of Dextrose	Two Hours After Injection of Dextrose
O45	+	83.8	416.6	227.2	111.1
O76	+	88.5	416.6	384.6	157.5
O42	+	93.2	270.2	72.5	103.4
O85	+	77.2	392.2	234.0	113.6
O78	++	98.0	272.6	214.2	107.9
O33	++	92.0	329.6	92.6	90.9
O74	++	74.9	258.0	221.0	155.0
O62	+++	85.2	275.2	116.2	107.1
O72	+++	92.6	447.4	176.4	110.3
O69	+++	107.1	394.6	211.2	183.0
N41	+++	94.3	379.6	422.4	153.8
O95	++++	103.1	441.0	405.4	240.0
O51	++++	77.3	357.0	138.8	77.3
O79	++++	94.9	365.8	167.6	83.3
O98	++++	72.1	447.4	389.6	147.8
O91	++++	68.8	461.6	343.8	222.2
O71	++++	65.2	375.0	202.7	96.8
O67	++++	65.8	309.2	394.6	361.4
O49	++++	145.7	434.8	500.0	163.0

* The determinations were made according to the macroscopic method of Folin and Wu after intravenous injection of 5 Gm. of dextrose (20 cc. of a 25 per cent solution).

† One plus sign (+) indicates partial or complete paralysis of one limb; ++, partial or complete paralysis of two limbs; +++, partial or complete paralysis of more than two limbs, with the animal still able to sit up; ++++, complete paralysis and prostration.

In order to establish a basis for comparison, we again first determined the reactivity of the normal animal to excessive doses of dextrose in eight tolerance tests on an equal number of normal monkeys. The results obtained are given in table 1.

It appears that the figures reached within the first half hour after injection lie between 174.4 and 441. However, at the end of the first hour seven of the eight normal monkeys showed a blood sugar level well within the normal

range, i. e., below 125, and at the end of two hours the values for all animals had returned to normal or even subnormal figures. It follows from this that the normal monkey, as a rule, is able to eliminate from the circulatory system within one hour a dose of 5 Gm. of dextrose and that this process is invariably completed within two hours.

Dextrose tolerance tests were then carried out with the same technic on nineteen poliomyelitic monkeys in various stages of paralysis. The results obtained are given in table 2. It will be noted that there is a marked difference between monkeys suffering from experimental poliomyelitis and normal monkeys with respect to their ability to clear the circulatory system from the test dose of sugar. Of nineteen paralyzed animals, only three showed normal blood sugar levels at the end of the first hour, the remaining sixteen giving figures between 125 and 500. At the end of the second hour, ten animals had normal values, but nine still continued to show figures between 125 and 362. As the experiment

TABLE 3.—*Effect of Insulin on the Blood Sugar Level of Four Normal and Eleven Poliomyelitic Monkeys* *

Number	Type of Animal	Blood Sugar Level During Fasting	Blood Sugar Level	
			One-Half Hour After Injection of Insulin	One Hour After Injection of Insulin
Q8	Normal	98.0	102.5	67.8
Q9	Normal	88.8	54.4	59.6
Q1	Normal	90.9	50.6	69.7
Q3	Normal	79.0	45.7	65.8
Q6	Paralytic	102.6	54.0	61.3
Q10	Paralytic	85.1	53.3	42.5
Q11	Paralytic	106.9	43.7	33.0
Q12	Paralytic	109.3	42.5	33.0
Q7	Paralytic	106.4	40.0	45.7
Q15	Paralytic	114.3	91.3	54.0
Q16	Paralytic	84.0	62.5	57.1
Q2	Paralytic	105.8	61.9	47.6
Q26	Paralytic	93.9	40.0	61.2
Q88	Paralytic	85.1	48.8	93.4
Q63	Paralytic	81.6	87.7	62.5

* Determinations were made according to the macroscopic method of Folin and Wu after intravenous injection of 2 units of insulin.

was not prolonged beyond that time, we do not know how much time was required for these animals to reach normal values again. As in previous straight determinations of blood sugar, we were unable to establish any clearcut correlation between the extent or duration of paralysis and the degree of dextrose tolerance, even though it will be noted that the three highest levels of blood sugar two hours after injection of dextrose occurred among the severely paralyzed animals. The significance of the aforementioned data is further enhanced by the fact that in three instances in which dextrose tolerance tests were carried out in the same animal before and after infection the curve of elimination indicated invariably a retardation in the clearing of the blood.

Effect of Insulin in Poliomyelitic Monkeys.—Sensitiveness to the blood sugar-lowering effect of insulin was tested in a group of four normal monkeys and in another group of ten monkeys suffering from various degrees of paralysis. As the weight of these animals differed little from an average of 2,500 Gm., a standard dose of insulin, i. e., 2 units, was administered to both normal and poliomyelitic monkeys by the intravenous route. Determinations of blood sugar were made before giving the insulin and again one-half and one hour after the injection. The data are presented in table 3.

It may be seen from table 3 that there was no fundamental difference in the mode of response to insulin between normal and poliomyelitic monkeys. Of the four normal animals, three were distinctly hypoglycemic at the end of the first half-hour, and the same was true for nine of the ten paralyzed animals. Comparison of the one hour readings between the two groups reveals no material difference in the speed of the return to physiologic values for blood sugar.

COMMENT

The data presented in this paper demonstrate that poliomyelitic infection in monkeys is associated with a marked disturbance of the carbohydrate metabolism. This disturbance does not ordinarily become apparent in a deviation from the normal blood sugar levels under static conditions but manifests itself characteristically by a functional inability of the paralyzed animal to eliminate from the circulation a test dose of dextrose with the same speed as does the normal animal. The described inhibition of the clearing of the blood would not seem to depend on the lesions produced by the virus in the central nervous system, since the increased tolerance for dextrose is not directly related to either the extent or the duration of paralysis. These observations may therefore be taken to indicate a profound systemic involvement in experimental poliomyelitis, irrespective of and apart from the neurotropic activities of the etiologic agent. Unless it should be proved that the results are due to a changed reflex activity of the vegetative nervous centers, it seems preferable to interpret the derangement in carbohydrate metabolism as evidence of the occurrence of some dysfunction of the endocrine apparatus during the course of the infection.

In comparing the results obtained in poliomyelitis with those recorded for diphtheria, one is struck by certain analogies and certain dissimilarities. Obviously, both diseases lead to the same functional inability to eliminate a test dose of dextrose from the circulation. It might be said that this defect, in a way, is comparable to the functional blockade of the reticulo-endothelial system commonly observed in a host of infectious diseases. However, the mechanism of clearing the blood of injected particles or of sugar is evidently quite at variance, involving in one case the operation of phagocytic cells and in the other the setting into motion of a complicated series of metabolic processes regulated by the interaction of specific internal secretions. What serves to differentiate the disturbance of the carbohydrate metabolism in poliomyelitis from that previously described for diphtheria, on the other hand, is chiefly the fact that poliomyelitic monkeys apparently respond to insulin as well as do normal monkeys. Again, there is no evidence in poliomyelitis for the consistent occurrence of stationary high or low levels of blood sugar, as has been found in diphtheria, even though some of our paralyzed animals showed a marked antemortem rise.

In view of the complexity of the endocrine basis for the regulation of the carbohydrate metabolism under normal conditions, it seems hazardous to attribute the abnormal retention of dextrose in paralyzed monkeys to the dysfunction of one particular endocrine gland or system of glands. This problem can be solved only by systematic analysis of every one of the various component factors.

SUMMARY AND CONCLUSIONS

Determinations of blood sugar in monkeys suffering from experimental poliomyelitis reveal no significant deviation from the level observed in normal monkeys. However, in some paralyzed animals there occurs an antemortem rise.

Dextrose tolerance tests demonstrate the existence in poliomyelitic monkeys of a functional inability to eliminate from the circulatory system a test dose of sugar in the same length of time as do normal monkeys. This derangement in carbohydrate metabolism appears to be unrelated to either the duration or the extent of paralysis.

Poliomyelitic monkeys respond to the blood sugar-lowering effect of insulin as well as normal monkeys.

The data presented in this paper suggest that in experimental poliomyelitis there occurs a profound systemic involvement, irrespective of the neurotropic activities of the virus.

The analogies and differences between the deranged carbohydrate metabolism in diphtheria and that in poliomyelitis are discussed.

SUBSTANCES INVOLVED IN THE COAGULATION OF THE BLOOD OF THE NEW-BORN INFANT

IV. VARIATIONS IN THE FIBRINOGEN CONTENT IN THE NORMAL INFANT

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Studies of the substances involved in the coagulation of the blood of the new-born infant have been presented in previous communications from this department.[1] In the course of further experimentation in this field we became dissatisfied with the refractometric method for the determination of fibrinogen which we had previously used. Examination was made, therefore, of the plasma of another series of infants, and the fibrin values were determined by the micro-Kjeldahl method or by weighing the dried clots. The results of this investigation are presented here.

METHOD

Natural plasma was used to avoid the possible error caused by oxalate or citrate, which has been said to draw fluid from the cells and thus dilute the plasma.[2] From 4 to 6 cc. of blood was drawn through the fontanel or by puncture of the internal jugular vein into an oiled and chilled syringe. The blood was immediately transferred to a paraffined tube and placed in ice. In a large centrifuge cup packed with ice, the tube was centrifugated for ten minutes at high speed. A cold paraffined pipet was used to transfer the supernatant plasma to a second paraffined tube. From this tube from 0.3 to 1 cc. quantities of plasma were accurately measured into other paraffined tubes with a chilled but not paraffined pipet.

The plasma was allowed to stand in these tubes until clotting was complete. Thirty minutes at room temperature was sufficient for coagulation in most

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instances, but it was found that in an occasional case in which coagulation was prolonged (not included in this series because there were other evidences of abnormality) a longer period was necessary; consequently, in all but the very earliest experiments the tubes stood several hours at room temperature or thirty minutes at room temperature and overnight in the refrigerator. In the earlier experiments the tubes in which the clots were formed were not paraffined, but this was found to be an occasional source of error, as small amounts of fibrin may adhere to the glass when the clot is transferred. After coagulation was complete, the clot was thrown out on several layers of filter paper. The filter paper absorbed the fluid, leaving the fibrin as a thin film which could be floated off when the top layer of filter paper was dropped in a beaker of distilled water. The fibrin was left in the distilled water for ten minutes or longer and then picked up on a fine glass rod.

For determination of nitrogen this clot was pressed dry on filter paper and transferred to a micro-Kjeldahl tube, and the nitrogen was determined by the Koch-McMeekin modification of the micro-Kjeldahl method.[3] The amount of fibrin was calculated by multiplying the value for the nitrogen content by 5.9, since, according to Hammarsten, fibrin contains 16.91 per cent nitrogen.[4]

For determination by weight, the clot was placed in alcohol and in ether for at least ten minutes each; then it was placed on filter paper and dried in a desiccator in an incubator overnight. The clots were then weighed to the nearest 0.05 milligram.

In approximately two thirds of the determinations the results of which are reported here the plasma was not diluted before clotting. It was recognized that other proteins might be caught in the coagulum,[5] but in our earlier attempts to use the diluted plasma we were not successful in obtaining clots firm enough to be picked up without loss. Later, with a proper adjustment of the calcium concentration of the mixture, satisfactory clots were obtained from plasma diluted with an 0.85 per cent solution of sodium chloride. Comparison was then made of the weight of clots from undiluted plasma with that of clots from various dilutions. No difference was found in the weight of clots from 1 cc. of plasma whether diluted to 5, 10, 20 or 30 cc. The undiluted plasma does give slightly higher results than the diluted, however. In a series of thirty-one successive determinations the clots from undiluted plasma weighed on an average 2.3 per cent more than those from the diluted plasma. Since this would give an average error of less than 0.01 Gm. in our figures, it does not materially affect their value. Nevertheless, for the later determinations we adopted the following method for obtaining the clot: One cubic centimeter of plasma (0.5 cc. can be used) is accurately measured into a paraffined 50 cc. centrifuge tube with a round bottom. To this is added 4 cc. of an 0.85 per cent solution of sodium chloride and 0.3 cc. of a 2 per cent solution of hydrated calcium chloride (for 0.5 cc. plasma half these amounts are used). The clot is handled in the same manner. This procedure is

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4. Hammarsten, Olaf: Weitere Beiträge zur Kenntnis der Fibrinbildung, Ztschr. f. physiol. Chem. **28**:98, 1899.

5. Cullen, G. E., and Van Slyke, D. D.: Determination of the Fibrin Globulin and Albumin Nitrogen of Blood Plasma, J. Biol. Chem. **41**:587, 1920.

practically the same as that described by Gram[6] except that natural plasma is used. Duplicate and triplicate determinations of fibrin were made in all but a few instances.

The subjects selected for study were normal full term infants in good general condition. During the course of the investigation a change was made in the method of feeding in the ward for new-born infants. According to the earlier routine the infants were put to breast every four hours, after which the breast milk was supplemented up to ½ ounce (15 cc.) at each feeding the first day, 1 ounce (30 cc.) the second day, and ½ ounce (15 cc.) more each day up to 3 ounces (90 cc.). The supplementary feeding consisted of equal parts of milk and water with 3 per cent cane sugar. The majority of the babies studied were on this

TABLE 1.—*Fibrin Values for Ten Infants During the First Ten Days of Life* *

	Day of Life									
Infant	1	2	3	4	5	6	7	8	9	10
1	0.35	0.42	0.43	0.48	....	....	0.67	0.55	....	....
2	....	....	0.52	0.48	0.47	....	0.37	0.37	....	0.38
3	0.36	0.50	0.50	0.56	0.59	....	0.50	....	....	....
4	....	....	0.53	0.53	0.46	0.47	....	0.54	....	....
5	....	....	0.36	0.42	0.33	0.36	0.34	0.41	....	....
6	0.30	0.32	0.37	....	0.32	....	0.38	0.36	....	....
7	....	0.45	....	0.45	0.45	....	....	....	0.37	0.33
8	....	0.28	0.36	....	....	....	....	0.37	....	0.50
9	0.31	0.41	0.35	....	0.40	....	....	0.50	....	....
10	....	....	0.51	0.52	....	0.43	0.46	0.37	....	....

* The values in tables 1 and 2 are expressed in grams of fibrin per hundred cubic centimeters of plasma.

TABLE 2.—*Estimation of the Maximum, Minimum and Average Values for Plasma Fibrin During the First Ten Days of Life for One Hundred and Thirty-One Infants*

Day		1	2	3	4	5	6	7	8	9	10
Number of determinations		11	24	27	19	15	7	9	10	5	4
Values	Maximum	0.36	0.52	0.53	0.56	0.59	0.47	0.67	0.55	0.56	0.50
	Minimum	0.22	0.23	0.25	0.28	0.25	0.29	0.30	0.35	0.31	0.33
	Average	0.29	0.36	0.38	0.41	0.38	0.39	0.41	0.42	0.39	0.39

schedule. The second group were put to breast every four hours but received no supplementary feeding. They were given water after nursing until the mother's milk came in. These infants were practically on a starvation diet for the first four days.

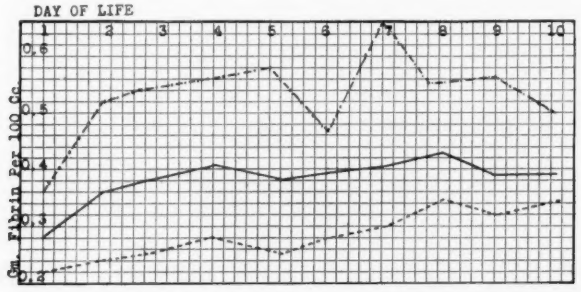
RESULTS

The results obtained on the two series of infants did not show sufficient difference to justify presenting them separately. The average figures for each of the first ten days from forty-three determinations on the second group were all between 0.04 and 0.06 Gm. per hundred cubic centimeters lower than the averages from eighty-eight determinations on the babies receiving supplementary food. Since this difference

6. Gram, H. C.: A New Method for the Determination of the Fibrin Percentage in Blood and Plasma, J. Biol. Chem. **49**:279, 1921.

was as great on the first day, before there could be any difference in the babies as a result of feeding, as it was later during the period, it seemed unjustified to attribute it to the diet. It is more probable that each series is too small in itself to give a reliable average; so the results from the two groups have been used to obtain the figures presented here, as representing the truer picture of the fibrin content during this period.

Table 1 shows the results of several determinations of fibrin on each of 10 different infants, demonstrating the variations which may occur in the individual child during this period. Table 2 summarizes the results of 131 determinations, giving the average, maximum and minimum values for fibrin found during the first ten days of life. These results are presented in graphic form in the figure.



Graphic representation of the maximum, minimum and average values for fibrin during the first ten days of life. The dot and dash line represents the maximum, the unbroken line the average, and the broken line the minimum.

COMMENT

The individual curves show considerable variation in type and demonstrate the changes in fibrin content possible from day to day. Several of them show what is brought out more clearly in the composite curve; namely, that there is in most cases a definite rise in the fibrin content during the first few days of life. After the fourth day there seems to be no consistent rise or fall, though individual infants may have curves in either direction. The average value for fibrin in the first ten days of life was found to be 0.38 Gm. per hundred cubic centimeters of plasma, with variations between 0.22 and 0.67 Gm. Ninety-two per cent of the figures fall between 0.25 and 0.55 Gm.

The exact relationship of fibrinogen to fibrin is still uncertain. Hsu and Wu [7] have found the quantity of fibrin formed by clotting to be in the neighborhood of 7 per cent less than the amount of fibrinogen

7. Hsu, C. H., and Wu, H.: Loss of Weight of Fibrinogen upon Coagulation, Chinese J. Physiol. **7**:117, 1933.

from which it was produced. Granting this difference, we are probably safe in assuming the value for fibrin to be an approximate indication of the quantity of fibrinogen in the circulating blood. The results of the present study indicate a lower fibrinogen content in the blood of the new-born than that found by the refractometric method, but the previous conclusion that there is a rise in the amount of fibrinogen during the first few days of life is supported here.

Bakwin [8] showed a similar rise in the protein content of the serum during this period in those infants who became dehydrated. The serum protein, however, decreased in concentration again as the dehydration disappeared during the latter part of the period, and the fibrin shows no such drop.

CONCLUSIONS

The quantity of fibrin formed in the plasma of infants during the first ten days of life has been studied. The average value for fibrin under the conditions of this investigation was found to be 0.38 Gm. per hundred cubic centimeters of plasma, with variations between 0.22 and 0.67 Gm. In the great majority of cases the content was between 0.25 and 0.55 Gm. There is commonly a rise in the amount of fibrin during the first three to five days of life, after which there is no consistent change.

952 N. Michigan Avenue.

8. Bakwin, H.: Dehydration in New-Borns, Am. J. Dis. Child. **24**:497 (Dec.) 1922.

Case Reports

ICTERUS GRAVIS NEONATORUM

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A case of severe neonatal jaundice of the icterus gravis group is described, with comment on the most important papers which have appeared since Diamond, Blackfan and Baty's [1] comprehensive report on erythroblastosis foetalis in 1932.

REPORT OF A CASE

A 3 week old girl was admitted to the children's service on Jan. 7, 1935. The family history was irrelevant except for the fact that the mother's father had died of tuberculosis when she was 7 years old and that she herself had had a cold abscess of the thigh, which was aspirated one and one-half years before the patient's admission. The first pregnancy, three years previously, resulted in the normal delivery of a full term stillborn child. It is not known whether the child showed jaundice or edema. Just before the termination of the present pregnancy the mother gave evidence of a beginning toxemia, with a blood pressure of 152 systolic and 102 diastolic and a trace of albumin in the urine. The baby was born in the maternity service on Dec. 17, 1934. Labor and delivery were easy. There was a large amount of amniotic fluid. The infant was not asphyxiated and had no convulsions or twitchings. The cry was vigorous. Physical examination gave normal results. The weight at birth was 7 pounds and 3 ounces (3,260 Gm.). Slight jaundice was noted on the first day. This increased and was present on discharge. The stools were always yellow. The infant had no fever during the stay in the hospital, and was discharged on the tenth day, weighing 6 pounds and 12 ounces (3,061 Gm.).

The patient was admitted to the children's service eleven days later, weighing 6 pounds and 4 ounces (2,834 Gm.). Two days previously the jaundice had begun to increase rapidly. The urine was dark. The baby refused her bottle.

The infant was somnolent on admission and desperately ill. The skin, scleras and mucous membranes showed the most extreme degree of jaundice. The tears were bile-stained. Pallor masked by icterus was evident. The liver was firm and extended down to the umbilicus. The spleen was not palpable. The neurologic examination and the rest of the physical examination, including that of the head, eyes, throat, ears, neck, chest, heart, lungs, abdomen, lymph nodes, skin and extremities, gave normal results. The blood count was: hemoglobin

From the Dr. Abraham Jacobi Division for Children, Lenox Hill Hospital, service of Dr. Jerome S. Leopold.

1. Diamond, L. K.; Blackfan, K. D., and Baty, J. M.: Erythroblastosis Fetalis and Its Association with Universal Edema of the Fetus, Icterus Gravis Neonatorum and Anemia of the Newborn, J. Pediat. **1**:269, 1932

(Sahli), 8.2 Gm. per hundred cubic centimeters (56 per cent); red cells, 2,000,000 per cubic millimeter; white cells, 18,150; polymorphonuclears, 50 per cent, 21 per cent of which were immature forms; lymphocytes, 48 per cent; monocytes, 1 per cent; eosinophils, 1 per cent. A few normoblasts were seen on smear. A transfusion of 80 cc. of citrated blood was given at once. An intravenous infusion of 100 cc. of a 10 per cent solution of dextrose and two clyses of Ringer's solution totaling 215 cc. were also administered that day. The infant would take nothing by mouth.

The next day, January 8, the jaundice was still extreme. The baby was critically ill. The blood count was: hemoglobin, 7.7 Gm. (53 per cent); red cells, 2,800,000; white cells, 29,000; polymorphonuclears, 53 per cent, 1 per cent of which were band forms; lymphocytes, 44 per cent and mononuclears, 3 per cent. There were 290 nucleated red cells per cubic millimeter (400 white cells counted). The Wassermann tests taken on this day and three days later gave negative results in both antigens. The Wassermann tests of the mother and father likewise gave negative results. A spinal tap was made. The Wassermann reaction of the spinal fluid was negative, and the icteric index, 2.5. The van den Bergh test of the spinal fluid gave negative results. Clyses and intravenous injections of a 10 per cent solution of dextrose were continued.

On the following day the baby was less somnolent, but the icterus was just as severe, the icteric index being 202. Roentgenograms of the long bones were normal. The patient received another transfusion of 85 cc. of citrated whole blood. Clyses and infusions of dextrose were continued. On the fourth day, January 10, the baby's condition improved. She seemed less lethargic and jaundiced. The test for the fragility of the erythrocytes showed beginning hemolysis with a 0.4 per cent and complete hemolysis with a 0.3 per cent solution of sodium chloride. On January 11 a third transfusion of 60 cc. of citrated blood was given. From then on improvement was rapid. The blood count on January 12, five days after admission, was: hemoglobin, 16.1 Gm. (110 per cent); red cells, 5,700,000; white cells, 12,400; polymorphonuclears, 19 per cent, 1 per cent of which were band forms; lymphocytes, 62 per cent; lymphoblasts, 2 per cent; monocytes, 12 per cent; eosinophils, 5 per cent; reticulocytes, 2.8 per cent.

The improvement continued progressively until the patient's discharge on January 27, twenty days after admission. The icterus receded. On January 14, the icteric index was 100; on January 22, 62 and on January 26, 28. There was still some jaundice visible when the patient was discharged. The liver became smaller, but it was still 2 fingerbreadths below the costal margin when the infant left the hospital. At no time was the spleen palpable. On the third day, there was a rise in temperature to 102.4 F., occurring after a transfusion and lasting only four hours. Otherwise the course was afebrile. The stools were always colored and contained bile. In the early part of the illness at the hospital the dark-colored urine showed albumin (4 plus), an occasional hyaline cast and bile. Later the urine became normal. The baby took a diet of breast milk, skimmed milk and evaporated milk increasingly well. The blood count on January 17, ten days after admission, showed: hemoglobin, 13.9 Gm. (95 per cent); red cells, 4,500,000; white cells, 6,900; polymorphonuclears, 37 per cent; lymphocytes, 56 per cent; monocytes, 6 per cent; eosinophils, 1 per cent; reticulocytes, 4 per cent. On January 23, the hemoglobin content was 15 Gm. (105 per cent) and the red cells, 4,200,000. The infant was discharged on January 27, weighing 7 pounds and 12 ounces (3,515.3 Gm.).

She was seen in the outpatient department on March 12, 1935. She weighed 10 pounds and 9 ounces (4,791.1 Gm.) and was not jaundiced. The liver was

3 cm. below the costal margin. The spleen was not palpable. The infant lay on her side with her head in marked opisthotonos. The head could be brought forward, but there was some resistance. The baby was unable to hold up her head. The blood count was: hemoglobin (Sahli), 11 Gm. per hundred cubic centimeters (75 per cent); red cells, 4,360,000; white cells, 8,550; polymorphonuclears, 16 per cent, of which 2 per cent were immature; lymphocytes, 81 per cent; monocytes, 1 per cent; eosinophils, 1 per cent; basophils, 1 per cent.

COMMENT

The seven year returns of the Registrar General for England and Wales [2] listed 1,800 infants under 4 weeks of age as dying of jaundice without an obvious cause, such as sepsis or obliteration of the bile ducts. Hampson [2] stated the belief that most of these deaths were due to icterus gravis. This syndrome, now recognized as far from uncommon in infants, occurs in animals, according to Volhard [3] only in the new-born horse. It has been reported almost exclusively in the white race although cases in Japanese [4] and in Chinese [5] patients have recently been described.

Icterus gravis, universal edema of the new-born infant and one type of congenital anemia form a closely related triad characterized almost always by erythroblastosis and anemia. In icterus gravis the liver, spleen and kidneys and, to a lesser degree, the other organs reveal many embryonic blood islands, preponderantly erythroblastic but containing also leukoblastic elements. The sinusoids of the liver and the periportal spaces are frequently packed with many nucleated red cells in all stages of development. These widespread foci of extramedullary hematopoiesis (which have been described even in the connective tissue beneath the cutis vera [6]) are characteristic of this condition. The organism has reverted to the fetal mechanism for the manufacture of its blood cells. The few scattered erythropoietic foci found in normal infants and to a greater degree in premature infants cannot compare in amount and extent to the erythroblastosis of icterus gravis, which is closely comparable to the picture observed in a fetus from 20 to 24 weeks old.[7]

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2. Hampson, A. C.: Grave Familial Jaundice of the Newly Born, Lancet **1**:429, 1929.

3. Volhard, E., cited by von Gierke, E.: Fetal Blood Diseases, Klin. Wchnschr. **10**:2295, 1931.

4. Fujimori, H.: Icterus Gravis Familiaris, Jap. J. Obst. & Gynec. **16**:234, 1933.

5. Ku, D. Y., and Li, Y.: Fetal Erythroleukoblastosis and Malignant Icterus, Virchows Arch. f. path. Anat. **283**:62, 1932.

6. Lightwood, R., and Hawksley, J. C.: Histological Preparations from Cases of Icterus Gravis Neonatorum, Proc. Roy. Soc. Med. **26**:1369, 1933.

7. Lightwood, R., and Hawksley, J. C.: Icterus Gravis Neonatorum and Allied Diseases, Proc. Roy. Soc. Med. **27**:255, 1934.

Ferguson [8] made a histologic comparison between 9 premature and 6 full term infants dying of icterus gravis. Six of the premature infants showed a few foci of normoblasts with an occasional erythroblast in the liver and spleen. The infants with icterus gravis had the typical picture of massive extramedullary hematopoiesis. The difference was all the more striking because the infants with icterus gravis were born at full term.

The polygonal cells of the enlarged liver may be deeply stained with bile and severely damaged. Fatty degeneration, hazy outline and necrosis of the cells are frequently observed. A patient with icterus gravis may for a short time have clay-colored stools. This fact together with an immediate direct reaction to the van den Bergh test may cause the condition to be momentarily confused with congenital stenosis of the bile ducts. The retention jaundice may have several causes: [9] 1. The badly damaged liver cells may be unable to excrete the enormous quantity of bilirubin resulting from the excessive hemolysis. 2. The rapid and marked hemolysis may make the bile too viscid to pass through the smaller bile channels. 3. Accumulation of the viscid bile in the finer radicles may lead to coagulation with resultant bile casts.

The evidences of hemolysis are seen in the deposition of iron pigment in the Kupffer cells of the liver, the endothelial phagocytes of the spleen and the convoluted tubules in the kidney and in other organs. The bone marrow shows active production of red and white blood cells, although it cannot manufacture enough erythrocytes to compensate for those destroyed. Unable to shoulder the burden alone, the marrow, according to some authors, is assisted by the fetal blood-forming centers, which in the normal new-born infant have almost disappeared.

The syndrome of icterus gravis is characteristic and should be recognized early so that adequate therapy may be instituted. It is often familial, but many sporadic cases have been reported. There may be a history that several children in the family died of severe icterus or were born dead with hydrops congenita. De Lange [10] reported the case of twins, one with icterus gravis and the other with congenital edema. Either an infant is born with jaundice or it develops within the first twenty-four hours, in contradistinction to physiologic icterus neonatorum, which makes its appearance on the second or third day of life. The occurrence of jaundice in the first twelve hours should always cause concern. A clue to the nature of the condition may be obtained quite

8. Ferguson, J. H.: Erythroblastosis in the Newly Born, Am. J. Path. **7**:277, 1931.

9. Hawksley, J. C., and Lightwood, R.: Contribution to the Study of Erythroblastosis: Icterus Gravis, Quart. J. Med. **3**:155, 1934.

10. de Lange, C.: Icterus Familiaris Gravis and Hydrops Fetalis with Erythroleukoblastosis, Acta pædiat. **13**:292, 1932.

early from the deeply colored liquor amnii and the peculiar golden vernix caseosa.[11] This coloration has been explained[9] on the basis of fetal excretion in utero of bile-containing urine and is therefore more to be expected in infants already having jaundice at birth. The liver and spleen are almost always enlarged. The absence of splenic enlargement in the case reported is noteworthy.

Anemia masked by increasing jaundice is a rapid development. Hemolytic hyperchromic anemia is possibly as characteristic of all members of the triad as erythroblastemia. In fact Parsons, Hawksley and Gittins[12] classified them as erythronoclastic anemias of the neonatal period: (1) with hydrops foetalis, (2) with icterus gravis, and (3) without edema or icterus gravis (i. e., the congenital anemia with erythroblastosis described by other authors). In Abt's[13] case of icterus gravis, the amount of hemoglobin as calculated from the blood iron was greater than the amount of hemoglobin actually found by the Newcomer method. In normal persons the observed values for hemoglobin (van Slyke oxygen-combining method) should coincide with the values calculated from the blood iron. In my series[14] of normal children, the hemoglobin content determined by the Newcomer method was even somewhat greater than the values calculated from the blood iron. Abt's figures might be explained on the basis of a severe hemolytic process breaking down the hemoglobin molecule with resultant liberation of iron in the blood stream.

Erythroblastemia is defined as the presence of nucleated red cells in the blood in greater number than is normal for the age. It is characteristic of icterus gravis and allows a very early diagnosis to be made. The number of nucleated red cells in the blood of the normal new-born infant is usually not greater than 2,000 per cubic millimeter, although 5,000 per cubic millimeter may be taken as the top figure.[15] These cells usually disappear completely by the fourth to the sixth day.[16] In icterus gravis, the nucleated red cells may exceed 50,000 per cubic millimeter on the first and second days and still be present in small numbers after two or three weeks. In this case there were 290 normoblasts per cubic milli-

11. Clifford, S. H., and Hertig, A. T.: Erythroblastosis of the New Born, New England J. Med. **207**:105, 1932.

12. Parsons, L. G.; Hawksley, J. C., and Gittins, R.: The Hemolytic (Erythronoclastic) Anemias of the Neonatal Period, Arch. Dis. Childhood **8**:159, 1933.

13. Abt, A.: Erythoblastosis in Icterus Gravis Neonatorum, J. Pediat. **3**:7, 1933.

14. Sobel, I. P., and Drekter, I.: Determination of the Iron Content of the Blood in Children, Am. J. Dis. Child. **45**:486 (March) 1933.

15. Diamond, Blackfan and Baty.[1] Hawksley and Lightwood.[9]

16. Altzitzoglou, J.: Blood Picture in Icterus Neonatorum Familiaris Gravis, Monatschr. f. Kinderh. **58**:329, 1933.

meter on the twenty-second day. Nevertheless, and this is an important point which has not been stressed in the literature, cases of icterus gravis with marked erythroblastemia may show a rapid diminution or even disappearance of abnormal red cells from the peripheral blood. This applies to untreated infants as well as to those receiving transfusions. Lightwood and Hawksley [6] remarked that histologic specimens taken from patients dying at different ages show a diminishing degree of extramedullary hematopoiesis. This may be mirrored in the gradual disappearance of nucleated red cells from the blood during the first three weeks after birth. The small number of normoblasts found in the present case does not mitigate against the diagnosis, as the count was made in the fourth week. The erythroblastemia does not necessarily run parallel to the severity of the hemolytic process. Cases [17] of increasing jaundice with a decreasing normoblast count have been reported. In this instance the hemolytic process was at its greatest intensity during the fourth week at a time when the normoblasts numbered only 290 per cubic millimeter.

Absence of nucleated red cells late in the disease does not, therefore, exclude the diagnosis of the condition as icterus gravis but rather is to be expected. Moreover, in a few instances no normoblasts were observed in the blood, even though the count was made within a few days after birth. In Hart's [18] case an examination of the blood on the third day revealed no abnormalities of the red cells. In the case reported by MacClure,[19] a blood count on the eleventh day revealed no increase in normoblasts above the normal figures. Greenwald and Messer [20] described an infant with a definite familial history of jaundice who showed no erythroblastemia. In Altzitzoglou's cases the nucleated red cells disappeared by the seventh day.

The white blood cell count is usually increased. Cells of the myelocytic series may be seen in the blood smear. Eosinophilia [21] is not unusual.

Infants with icterus gravis not infrequently exhibit the peculiar somnolence observed in this case, or they may even have severe convulsions. In some of these infants postmortem examination reveals intracranial hemorrhages such as Lightwood and Hawksley [9] described, and in others,

17. de Lange, C.: Further Studies in Grave Familial Icterus, Jahrb. f. Kinderh. **142**:255, 1934.

18. Hart, A. P.: Familial Icterus Gravis of the New-Born and Its Treatment, Canad. M. A. J. **15**:1008, 1925.

19. MacClure: Icterus Neonatorum Gravis, Ztschr. f. Kinderh. **51**:86, 1931.

20. Greenwald, H. M., and Messer, W.: Icterus Neonatorum Gravis, Am. J. M. Sc. **174**:793, 1927.

21. Collis, W. R. F.: Icterus Gravis Neonatorum, Irish J. M. Sc. **99**:106, 1934.

kernicterus,[22] a condition which is limited to the first days of life and occurs almost exclusively in icterus gravis. Obstructive jaundice of the greatest severity, such as congenital stenosis of the bile ducts, has yet to yield kernicterus. The term was coined by Schmorl in 1903, but it was Orth who first described the lesion, twenty-eight years before that.[23] The basal ganglia are deeply stained and stand out strikingly on microscopic examination. The caudate, lenticulate, subthalamic and dentate nuclei, the thalami, the mamillary bodies and the cornu ammonis are involved chiefly.[23] The degenerated ganglion cells and myelin sheaths contain bile pigment. Most authorities [23] are of the opinion that bile lodges in previously damaged nerve tissue just as an intravital dye will localize in zones of injury. Nuclear icterus is responsible for a certain proportion of the deaths occurring before the fifth day. It may manifest itself in respiratory paralysis, convulsions, drowsiness or extrapyramidal spasticity. Patients who have recovered may exhibit mental retardation or sequelae referable to the central nervous system at a later date, as was seen in the case described here. In de Lange's [17] fourth case the patient still had a peculiar opisthotonos six months after birth. Autopsy revealed bronchopneumonia as the cause of death, but meningitis was not present. The globus pallidus and the putamen showed toxic degeneration, which de Lange interpreted to be the result of kernicterus. This peculiar opisthotonos, which in the presence of some intercurrent infection may arouse suspicion of meningitis, was beautifully demonstrated in the present case.

Wilson [24] in his classic paper published over twenty years ago cautiously pointed out the analogy between his syndrome and the newly described kernicterus of Schmorl. Recently several investigators [25] have again discussed a possible relationship between nuclear jaundice and Wilson's disease; that is, bilateral symmetrical softening of the lenticular nucleus with cirrhosis of the liver.

The similarity of the localization of the cerebral lesions, the familial tendency and the hepatic changes in the two conditions is striking. Lightwood and Hawksley [26] recently demonstrated a fine fibrosis of the liver in infants dying late in the course of icterus gravis. They raised the question as to whether icterus gravis by virtue of the selective staining

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22. Monahan, D. T.: Kernikterus: Jaundice of the Nuclear Masses of the Brain, Yale J. Biol. & Med. **5**:523, 1933.

23. Zimmerman, H. M., and Yannet, H.: Kernikterus: Jaundice of the Nuclear Masses of the Brain, Am. J. Dis. Child. **45**:740 (April) 1933.

24. Wilson, S. A. K.: Progressive Lenticular Degeneration: A Familial Nervous Disease Associated with Cirrhosis of the Liver, Brain **34**:296, 1912.

25. (*a*) Lightwood and Hawksley,[7] (*b*) Zimmerman and Yannet.[23] (*c*) Lightwood, R., and Hawksley, J. C.: Icterus Gravis, Arch. Dis. Childhood **8**:364, 1933.

26. Footnotes 9, 7 and 24.

of the basal ganglia occurring in a small proportion of cases and these hepatic changes may not be the etiologic basis for the hepatolenticular degeneration described by Wilson. Zimmerman and Yannet,[23] on the other hand, noted that Wilson's disease occurs only in adults, that patients with this condition give little evidence of a lesion existing since infancy and that although jaundice may occur the basal ganglia are never pigmented. They concluded that there are more differences than similarities between these two conditions, which are not causally related. Nevertheless, the analogy is so pronounced that one is forced to speculate as to whether the future may not reveal some connection between icterus gravis and Wilson's disease.

A debated question about icterus gravis is whether the erythroblastosis is primary or compensatory. One group of investigators, including Abt [13] and Diamond, Blackfan and Baty,[1] have stated that the disease is a disturbance of the metabolism of the hematopoietic system, a primary overgrowth of erythroblastic tissue. The other view, upheld by Parsons [12] and by Lightwood and Hawksley,[9] is that embryonic hematopoiesis is a symptom and not a cause of the disease. It is a response to an increased call for red blood cells. This call is the result of excessive hemolysis. Neither theory explains all the facts. In addition, the compensatory theory does not give the underlying cause for the hemolysis, and the primary theory offers no basic reason for the erythroblastosis.

The prognosis has been considered very grave. However, many patients with icterus gravis, especially those with a mild form, have recovered without treatment. With early and vigorous therapy the outlook should now be much brighter.

The treatment consists primarily of early and frequent blood transfusions. They appear not to arrest hemolysis [25] but rather to tide the infant over a period of severe anemia until the hemolytic process ceases spontaneously. In the present case, three transfusions produced dramatic improvement. The hemoglobin content rose from 8.2 to 16.8 Gm. per hundred cubic centimeters in five days, and the infant made a rapid recovery. The results were all the more gratifying since the patient was seen so late in the course of the disease. Hampson,[2] who formerly gave serum intramuscularly, has now become convinced that prompt repeated transfusions represent the only real method of treatment.[27] The importance of blood transfusions in cases of icterus gravis cannot be emphasized too strongly. Infusions of dextrose may be administered to spare the damaged liver cells. Intramuscular injections of liver extract, advocated by some authors,[27] were found by Collis [21] to be ineffectual.

27. Hampson, A. C.: Jaundice in the Newly Born, Practitioner **131**:59, 1933.

CONCLUSION

A case of icterus gravis neonatorum with intense jaundice, hyperchromic anemia and slight erythroblastemia is described. The hemolytic process attained its maximum intensity during the fourth week.

Infants with icterus gravis show a decreasing nucleated red blood cell count with increasing age. Late in the disease the erythroblastemia may be slight or absent.

Present concepts of icterus gravis are discussed.

TUBERCULOSIS OF THE ADRENAL GLANDS IN A CHILD OF TWELVE, WITH NECROPSY

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Tuberculosis of the adrenal glands is one of the very unusual conditions encountered in medical practice. The following statistical data will serve to emphasize this fact. Of 696,789 patients admitted to the Mayo Clinic [1] from 1908 to 1929, only 108 suffered from this condition. During 1926, 391 deaths occurred throughout the United States from Addison's disease, or 1 case for every 250,000 of the population. Guttman's [2] findings on the incidence of this disease in Minnesota for the year 1924 closely approximate these figures.

During childhood tuberculosis of the adrenals may be regarded as distinctly rare. Monti [3] found among 200 cases of Addison's disease only 6 in children under the age of 13 years. Greenhow's [4] figures show only 4 of 330 cases to have occurred during childhood, or a ratio of 1 to 62. Guttman [2] estimated that about 3.45 per cent of all cases are encountered in children under 10. Langmead [5] stated that not a single case of this disease has been recorded in the annals of the Hospital for Sick Children at Great Ormond Street. Up to 1913 Comby [6] was able to collect from the literature reports of only 21 cases occurring in childhood; Dezirot [7] found mention of only 48 cases in children under 16 years, and of these only 6 were in children under 10. The more recent literature, especially that emanating from American sources, contains surprisingly few references to this subject. Pediatric textbooks are prone to treat the subject in an exceedingly sketchy fashion. Indeed

1. Rowntree, L. G., and Snell, A. M.: A Clinical Study of Addison's Disease, Philadelphia, W. B. Saunders Company, 1931.

2. Guttman, Paul H.: Addison's Disease: A Statistical Analysis of Five Hundred and Sixty-Six Cases and a Study of the Pathology, Arch. Path. **10**:742 (Nov.) 1930.

3. Monti, cited by Felberbaum, D., and Fruchthandler, E. A.: Addison's Disease in Children with Report of a Case, New York M. J. **86**:256 (Aug. 10) 1907.

4. Greenhow, cited by Felberbaum, D., and Fruchthandler, E. A.: Addison's Disease in Children with Report of a Case, New York M. J. **86**:256 (Aug. 10) 1907.

5. Langmead, Frederic: A Case of Addison's Disease in a Boy, Aged Ten Years, Lancet **1**:499 (Feb. 15) 1913.

6. Comby, cited by Rowntree and Snell.[1]

7. Dezirot, cited by Rowntree and Snell.[1]

one authority [8] made the astounding assertion that Addison's disease does not occur during childhood.

These circumstances, I believe, warrant the report of the following case, which may be considered as all the more remarkable because of the persistent absence of pigmentation, regarded as one of the cardinal signs of this disease.

REPORT OF A CASE

C. R., a boy 12 years and 10 months old, was admitted to the Children's Hospital on Nov. 15, 1933, complaining of anorexia, weakness and dizziness of about six months' duration and of nausea and vomiting of several weeks' standing.

The father and mother and six brothers were living and well. There was no history of miscarriage or of tuberculosis in the family.

The patient had had measles, pertussis and recurrent attacks of tonsillitis. He had never possessed a robust constitution but had been able to participate unrestrictedly in the usual activities of boyhood. Because of laxity of parental training, the patient's mode of living had been largely governed by his own whims and impulses.

During the six months prior to his admission the patient complained of being tired and showed some disinclination for play. His appetite became impaired, and he lost considerable weight. He complained of dizziness and headaches. During the past few months the character of his school work showed striking depreciation. More recently, he became subject to attacks of nausea and vomiting, frequently precipitated by a change to the upright posture.

Examination on admission disclosed an alert, intelligent and cooperative lad of about 12, unusually voluble and inordinately eager to expatiate on his complaints. His development was normal, and his nutrition, somewhat below par. He did not appear especially ill. The eyes, ears and nose were normal. The mouth was normal; the teeth were not decayed; the tongue was moist and slightly furred, and the tonsils were small and not infected. The nasopharynx showed a moderate amount of mucopurulent secretion. There was no adenopathy. The contour of the chest was normal. The heart presented no abnormalities; the pulse rate appeared well sustained (84 per minute). The abdomen was soft, not tender, and the spleen and liver were not palpable. The genitalia were normal. The nervous system was normal save for the absence of the knee jerk reflex and the presence of a suggestive Kernig sign. On attempting to stand he complained of dizziness and his weakness became apparent. The skin over the back was dry and reddish, and the palmar surface of the tips of the fingers was dry, cracked and denuded of epidermis and somewhat tender. The toes presented a similar picture, though to a less marked degree. The temperature and the respiratory rate were normal. The Mantoux test with 0.1 mg. of tuberculin resulted in a markedly positive reaction.

The history and the results of the physical examination suggested the following diagnostic possibilities: neurosis, tuberculosis, lesions of the cord, toxic neuritis, sinusitis, hypoglycemia and a labyrinthine disorder.

Clinical investigations were undertaken to establish the cause of his disability. The urine was normal. The blood count disclosed a hemoglobin content of 80 per

8. Morse, John L.: Clinical Pediatrics, Philadelphia, W. B. Saunders Company, 1926, p. 782.

cent (Dare), 4,250,000 erythrocytes and 11,600 leukocytes, with 31 per cent polymorphonuclears, 66 per cent lymphocytes, 1 per cent large mononuclears and 2 per cent basophils. The coagulation time was three minutes. A roentgenogram of the chest revealed pulmonary tuberculosis of the incipient and quiescent type, involving chiefly the upper lobe of the right lung. The hili showed increased fibrosis. The antrums and the ethmoid sinuses were the seat of moderate infection, with no evidence of retention, however. The Wassermann reaction of the blood was negative. The spinal fluid contained: 13 cells per cubic millimeter; the sugar content was normal; the protein content was 18 mg. per hundred cubic centimeters, with a slight increase in globulin; the colloidal gold and the Wassermann reactions were negative. The sugar content of the blood was 85 mg. per hundred cubic centimeters, with a normal sugar tolerance curve. The blood pressure was 90 systolic and 45 diastolic.

In the course of the next few weeks the following opinions were rendered by various members of the attending staff: The eyegrounds were pronounced normal by Dr. Ralph Danielson. Dr. H. L. Hickey found no labyrinthine involvement. Dr. J. Hutton stated the belief that the conditions of the skin was the expression of mild ichthyosis or possibly of xerosis. Dr. Daniels failed to find evidence of a pathologic process in the nervous system. On December 12 my progress notes disclosed the observation that there might conceivably be some disturbance of the function of the adrenal glands.

During his sojourn at the hospital the patient maintained an unfailingly cheerful demeanor which did not wholly desert him even during periods of profound mental and physical depression. He passed most of his time in bed. For perhaps brief periods for two or three days he would spend a part of the day in a wheelchair or would stroll about the ward. For a brief spell in January he was able to attend the grade school and the church services at the hospital. He delighted in reading, playing games and fraternizing with his fellow patients. His mental faculties remained unimpaired to the last. There was a steady though gradual loss of strength, interrupted now and then by astonishing return of physical vigor. Even during the earlier weeks of hospitalization he was subject to overpowering spells of exhaustion, during which he was barely able to raise his head or arms and his voice would become almost inaudible from sheer weakness. Such profound asthenia would last from several hours to several days. The loss in weight paralleled the impairment in strength.

His appetite was usually very poor, and frequently he showed a positive aversion for food. Then again he would ask for food notoriously difficult to digest and consume it with relish and without unpleasant after-effects. Not infrequently no food would be accepted for several days in succession. Nausea and vomiting were outstanding symptoms. It was unusual for two or three days to pass without emesis having taken place. Eructations were not noted. The patient was moderately constipated, but the character of the stools indicated normal digestion. Abdominal distention was not complained of, and palpation revealed no masses or enlargement of the liver or spleen.

The respiratory rate was usually normal; cough and dyspnea were absent, and examination of the lungs yielded uniformly negative results. Very soon after admission, the cardiac action was found to be feeble, and this was particularly noticeable on the slightest exertion. A change to the erect posture would cause the patient to become pale, faint, dizzy and almost pulseless. Elevation of the arm would frequently cause the disappearance of the radial pulse. At times

and for variable periods, this circulatory asthenia would be much less apparent. The heart showed no enlargement, and no murmur; the sounds were feeble, and the rate varied from 84 to 120 with the patient in a recumbent position. Palpitation was not complained of. The blood pressure range was from 60 to 74 systolic, with an average of 40 diastolic. The temperature range was from 97 to 99 F.

Shortly after admission marked tenderness of the toes was complained of. The very lightest touch would cause a sharp outcry. At about the same time he complained of pain of moderate severity in the abdomen. During attacks of overwhelming weakness he preferred to be left alone and would lapse into a state of drowsiness from which he could be aroused with ease. He was never restless or irritable. Only during the terminal stage of his illness was there any clouding of mental alertness.

The erythema and desquamation present on admission gradually cleared, were gone in about three weeks and did not recur. Neither the mucous membrane nor the skin presented at any time any discoloration which could conceivably be interpreted as addisonian pigmentation.

At no time did he present symptoms referable to the urinary system.

Repeated urinary examinations disclosed no abnormalities aside from a few pus cells. During the last five weeks of life a faint trace of albumin and a few hyaline and a little later waxy casts appeared. The specific gravity showed fixation between 1.011 and 1.014. The hemoglobin content of the blood fluctuated between 65 and 52 per cent; the erythrocyte count, from 3,500,000 to 2,750,000, and the leukocyte count, from 13,000 to 7,400 without evidence of abnormal cells. The basal metabolic rate registered minus 8. The blood sugar on December 12 was 108, and the test for sugar tolerance gave a normal curve. A roentgenogram of the abdomen revealed no calcification. A second roentgenogram of the chest, taken on March 24, showed small calcified lymph nodes indicative of tuberculosis in childhood.

During the last week of life, the patient ate very little, and fluids were supplied by gavage and parenterally. Although his general condition was not appreciably altered, it did not appear to portend an early death. On March 26 he became drowsy and was aroused with some difficulty. On March 27 at 9 p. m. his pulse was found to be very weak; the extremities were cold, and a considerable degree of cyanosis was present. His condition grew steadily worse, and at 2:45 a. m. on March 28 the pulse was imperceptible. He became very restless, excited and irrational, and respirations became very rapid and shallow and subsequently dropped to 3 per minute. The patient died at 4:15 a. m.

Treatment during the early stages of hospitalization had consisted of supportive measures, a blood transfusion on three occasions and sedatives when indicated. When vomiting became uncontrollable, fluids were supplied by extra-oral routes. When anorexia was extreme, gavage was resorted to for several days at a time. As soon as the true nature of the malady was suspected, an extract of adrenal cortex was administered daily, and its administration was continued with occasional interruption throughout the duration of his life. The extract appeared to afford considerable improvement for a time and engendered the hope that life might thereby be appreciably prolonged.

Autopsy was performed by Dr. E. I. Dobos, and the salient findings are herewith appended. The body was that of a well developed, poorly nourished boy of about 12 years of age, showing no significant changes of the skin. No areas of caseation or calcification were found in the parenchyma of the lungs. The hili and the peribronchial glands were considerably enlarged, with fusion of

capsules. A cross-section of these glands showed areas of scar tissue but no caseation. No noteworthy findings were encountered in the abdominal cavity.

Both kidneys were moderately enlarged and edematous. The adrenal glands were considerably atrophied. The medullary substance had almost disappeared. The cortex was the seat of innumerable small yellowish nodules, varying in size from 1 to 5 mm. in diameter. A guinea-pig inoculated with an emulsion of the adrenal gland revealed tuberculous foci of the miliary type in practically all the abdominal viscera. Microscopic examination disclosed small necrotic foci in the adrenal cortex surrounded by round plasma and fibroblast cells, epithelioid cells and large numbers of giant cells. Complete disappearance of cortical and medullary substance was found in scattered areas. The lymph nodes were dotted with miliary tubercles.

SUMMARY AND COMMENT

The case of a boy of 12 with tuberculosis of the adrenal glands, in all probability secondary to involvement of the bronchial lymph nodes, who lived about ten to twelve months after the presumptive onset, is reported. The symptoms were strikingly like those encountered in the average case of Addison's disease in an adult. However, pigmentation, regarded as the most striking visible manifestation of the pathologic process and present in all but one of the cases comprising the series observed at the Mayo Clinic, was at no time detected on the skin or on the mucous membranes. The true nature of the malady was suspected only after a period of observation of about four weeks, chiefly on the basis of the profound asthenia, marked circulatory weakness and persistence of anorexia, nausea and vomiting. An extract of adrenal cortex afforded a fair measure of temporary relief. Convulsions, commonly noted in the terminal stages of tuberculosis of the adrenal glands in childhood, were not present. Death, due to circulatory failure, supervened rather unexpectedly. Necropsy confirmed the diagnosis.

It is not improbable that tuberculosis of the adrenal glands is not so infrequent an occurrence in childhood as the scarcity of reports in the literature would lead one to believe. Greater familiarity with its symptomatology would doubtless lead to its more frequent recognition.

326 Republic Building.

PRIMARY TUBERCULOSIS, OBSTRUCTIVE PULMONARY EMPHYSEMA AND ASTHMA WITH RECOVERY

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The occurrence in infancy of tuberculosis, obstructive pulmonary emphysema or asthma, singly, is relatively common. But a primary tuberculous infection causing obstructive pulmonary emphysema and asthma, with recovery, in an infant 9 months old is rare. In fact, a search of the literature failed to disclose a report of such a sequence of events. It was therefore considered advisable to record the following case.

REPORT OF CASE

History.—E. S., a white boy, was born at term on Nov. 7, 1927. Two other children in the family were living and well. He was nursed for two months and then placed on a diet of diluted pasteurized grade A cow's milk, supplemented with orange juice and cod liver oil. He vomited continuously until given whole lactic acid milk. Progress was satisfactory until February 1928, when he caught cold while the house was being painted. He acquired a mild cough, which continued until May, when the mother noticed for the first time that he wheezed. His physician made a diagnosis of bronchial asthma. He was not relieved by inhalations of steam or administration of benzyl benzoate or epinephrine. Oatmeal, Cream O'Wheat and a corn-starch mixture had been added to his diet. The patient was seen by me on Aug. 23, 1928.

Examination.—The subject was a thin, somewhat pale infant of 9 months, obviously distressed by asthmatic wheezing, which was audible throughout the room. The percussion note seemed hyperresonant, perhaps a bit louder on the left side. The chest was filled with sibilant and sonorous râles. The patient weighed 14 pounds and 7 ounces (6,548.7 Gm.). Cutaneous tests elicited the following reactions: 2+ to wool and goose feathers; 1+ to orris root, dog hair, rabbit hair and oat. There were no reactions to wheat, egg yolk and egg white, milk, casein, chicken feathers, rice, corn and the hair of cattle. Physical examination showed the patient to be normal in other respects.

Course.—The room was thoroughly cleaned; a cotton mattress replaced the hair mattress of his crib, and a kapok pillow was substituted for the feather pillow. The patient was given a diet of scraped beef, broths, Cream O'Wheat, toast, orange juice and whole cow's milk. Despite these measures he continued to wheeze. He was afebrile, but in the next two weeks he lost 13 ounces (368.6 Gm.) and appeared weaker. Roentgen examination was made on September 10 (fig. 1).

The patient was sent immediately to the Chevalier Jackson Bronchoscopic Clinic of Philadelphia. Roentgen findings on his admission were similar to those

reported by Dr. W. P. Howard. Diagnostic bronchoscopic examination was performed by Dr. Louis H. Clerf on Sept. 17, 1928, who offered the following report of the case:

"The larynx and the upper part of the trachea appeared normal. The carina was shortened from the front backward and was irregular in outline and broader than normal; there was marked widening of the angle of bifurcation of the trachea. The orifice of the left main bronchus was stenosed, the result of displacement outward of the inner bronchial wall; in the right main bronchus at the

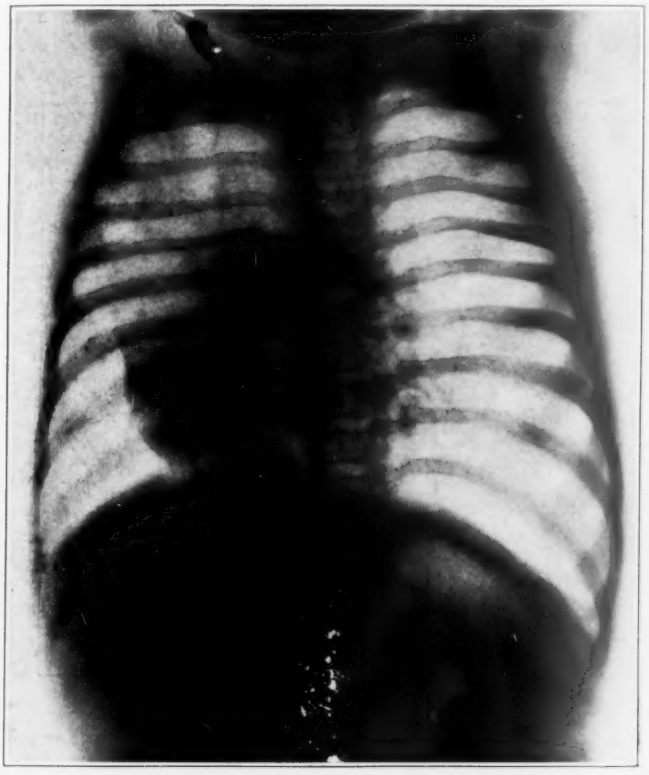

Fig. 1.—Roentgenogram showing marked emphysematous changes in the left lung, with complete displacement of the heart toward the right and downward displacement of the left leaf of the diaphragm. The interspaces on the right side of the chest are very much smaller than the corresponding ones on the left. These changes suggest an obstructive emphysema, probably due to a foreign body lodged in the opening of the left primary bronchus. Lateral, postero-anterior and anteroposterior roentgenograms did not show any visible foreign body, probably it was some substance which was not visible with roentgen radiation.

offshoot of the bronchus of the upper lobe of the right lung there was found an irregular mass springing from the inner wall; this was not inflamed or ulcerated and appeared to be pale granulation tissue; it felt very firm when

palpated with forceps; a specimen of secretion was removed for bacteriologic study. The bronchoscopic diagnosis was: compression stenosis of the left main bronchus; neoplasm (?) in the right main bronchus; widening of the angle of bifurcation of the trachea (fig. 2).

"At a bronchoscopic examination on October 3, a small growth in the right bronchus was removed for histologic examination, and additional secretion was secured for bacteriologic study. The tissue was evidently inflammatory and contained atypical giant cells, so that the lesion was suggestive of tuberculous infection. In the secretion removed bronchoscopically tubercle bacilli were found. The entire growth in the right bronchus was removed and at a subsequent bronchoscopic examination there was no evidence of recurrence.

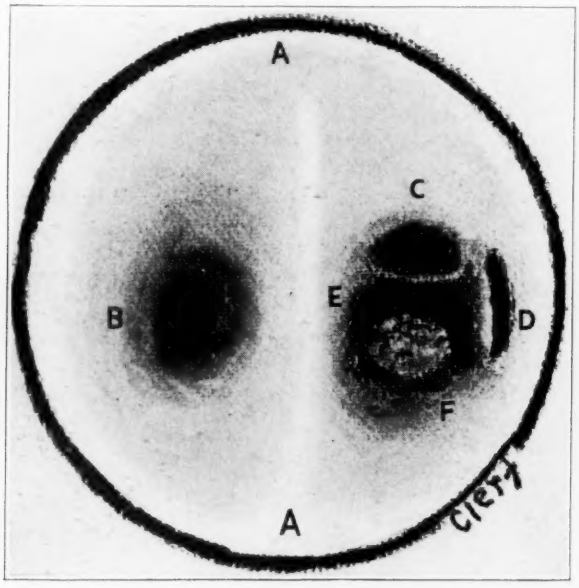

Fig. 2.—A composite view of the bronchoscopic findings showing stenosis of the left bronchus, with a small tuberculoma in the bronchus of the lower lobe of the right lung. The symbols used are: *A-A*, the carina; *B*, the left main bronchus, which is greatly narrowed; *C*, the bronchus of the middle lobe of the right lung; *D*, the bronchus of the upper lobe of the right lung; *E*, the bronchus of the lower lobe of the right lung with a small tuberculoma (*F*) springing from the posterior wall.

"The Wassermann test was negative.

"The patient made a very satisfactory recovery over a period of several months, and at a bronchoscopic examination performed on June 10, 1929, the right bronchus appeared practically normal. The left bronchus still was slightly narrowed, and the carina remained wider than normal. The patient was discharged on June 21, 1929. At that time there was very striking improvement, including a marked gain in weight.

"The left bronchus was concentrically narrowed owing to a crowding in of the walls. This unquestionably was due to some extrabronchial lesion, probably to enlargement of the lymph nodes. The carina was markedly widened owing to enlargement of lymph nodes at the bifurcation of the trachea.

"The small growth in the right bronchus was probably a tuberculoma, for it presented characteristics not unlike those of a tuberculous lesion. When discharged from the hospital the growth had disappeared, and there was definite improvement in the appearance of the left bronchus.

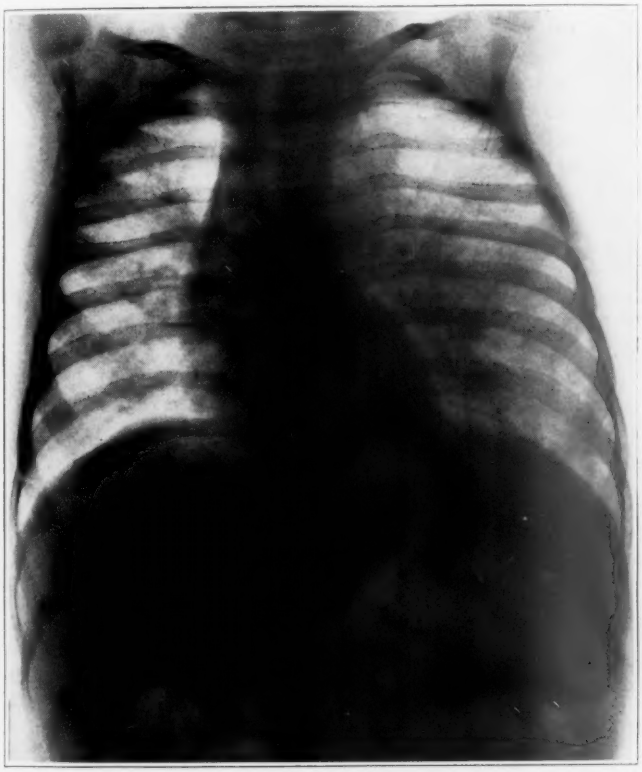

Fig. 3.—Roentgenogram taken on Dec. 6, 1928, which records a very remarkable change. The heart has gone back toward the left side. There is some cloudiness of the left lung, which is functioning now, whereas formerly it was definitely overdistended. There is apparently some exudate in the left lung.

"This was an unusual case, for it presented certain features that are not commonly observed and are extremely rare in one patient. I have noted a number of cases of stenosis of a bronchus resulting from enlargement of the peribronchial lymph nodes of tuberculous origin. In this case there was definite evidence of enlargement of the peritracheal lymph nodes at the tracheal bifurcation. There was also enlargement of the lymph nodes about the left main bronchus producing bronchial stenosis. The stenosis was sufficient to cause a very high degree of

obstructive emphysema. In the right bronchus there was a small tuberculoma. The amazing part was that the patient made a very satisfactory recovery."

Subsequent Course.—The boy was seen again by me on Sept. 16, 1930, and on Sept. 7, 1931. At the latter visit his height was 40 inches (101.6 cm.) and his weight, 32½ pounds (14.8 Kg.). He was tall, thin and ruddy-cheeked, with bright eyes, an active mind and abounding energy. An intracutaneous test with 0.1 mg. of tuberculin gave strongly positive results. The roentgenologist reported: "The volume of the right side of the chest is larger than that of the left. The interspaces on the left side are narrower than the corresponding ones on the right. There is a slight total dorsolumbar scoliosis, with convexity to the right. No definite calcification is visible in the hilus of either lung. The markings in the region of the roots are rather extensive and dense. There are no parenchymal changes suggesting tuberculosis."

In March 1933, the patient successfully weathered a moderately severe attack of measles followed by whooping cough, the only illnesses since his discharge from the clinic in Philadelphia.

Repeated inquiries concerning contact with persons having tuberculosis were fruitless until June 1933. An uncle, a frequent visitor in the home for years, was discovered to have an old unhealed, active tuberculous lesion in the chest. In all probability he was the source of this patient's tuberculous infection.

817 Madison Avenue.

CALCIFICATION OF THE CHOROID PLEXUS

REPORT OF A CASE IN A CHILD AGED FOUR YEARS

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Calcification of the choroid plexus in children has not been described hitherto in the pediatric literature. The neurologist and the roentgenologist have been made aware of the condition and its significance by the reports of Heuer and Dandy,[1] Dyke [2] and Beals [3] and, more recently, of Dyke and Davidoff.[4] The roentgenograms for the case described herein were shown to a number of pediatric authorities who not only had never seen such a case but were unacquainted with the findings of the foregoing observers. It therefore seemed desirable to report this case as one of pediatric interest.

A brief anatomic consideration of the choroid plexus is of interest. The following paragraph is quoted from Dyke and Davidoff: [4]

> These structures [the choroid plexuses] are largest in the two lateral ventricles, but are also present in the third and fourth ventricles. In the lateral ventricles they occupy the grooves between the basal ganglia and the thalami (sulci chorioidei) on the ventricular floor, and converge anteriorly, fusing after they pass through the foramina of Monro. Posteriorly they diverge until the bodies of the ventricles are about to divide into the posterior (occipital) and inferior (temporal) horns. There each plexus makes a sharp turn and follows the ventricle around the pulvinar into the inferior horn. The portion of the plexus when the bend occurs is called the glomus. At this point the plexus tissue is most abundant. No choroid exists in the frontal or occipital horns.

It is at the bend of the plexus, or the "glomus" referred to in the quotation, that deposits of calcium salts most frequently occur. Calci-

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From the A. Jacobi Division for Children, Service of Dr. Jerome S. Leopold, the Lenox Hill Hospital.

1. Heuer, G. J., and Dandy, W. E.: Roentgenography in the Localization of Brain Tumor, Based upon a Series of One Hundred Consecutive Cases, Bull. Johns Hopkins Hosp. **26**:311, 1916.

2. Dyke, C. G. : Indirect Signs of Brain Tumor as Noted in Routine Roentgen Examinations: Displacement of the Pineal Shadow, Am. J. Roentgenol. **23**:598 (June) 1930.

3. Beals, J. A.: An Intracranial Calcification, Probably of Choroid Plexus, Radiology **15**:268, 1930.

4. Dyke, C. G., and Davidoff, L. M.: The Demonstration of Normal Cerebral Structures by Means of Encephalography: I. The Choroid Plexuses, Bull. Neurol. Inst. New York **2**:331 (July) 1932.

fication in the choroid plexus was first demonstrated roentgenographically by Schüller [5] and by Heuer and Dandy.[1]

INCIDENCE

From a study of a series of 2,723 roentgenograms of the skull Dyke [2] reported demonstrable calcification of the choroid plexus in 5.1 per cent of the cases. The incidence of calcification in his series varied with the sex and strikingly with the age of the patient. Calcification was present in 6.1 per cent of the males and in 4.1 per cent of the females (or a ratio of 3:2). The average incidence for both sexes up to the age of 40 was 2 per cent, whereas between the ages of 40 and 80 years it was 9.4 per cent. Up to the age of 40 the frequency of calcification was about equal in the two sexes. However, in the group between the ages of 40 and 80 years the incidence in the males was 12.2 per cent, whereas that in the females was 6.6 per cent.

An analysis of Dyke's original figures is of interest. Calcification of the choroid plexus was found in 5.1 per cent of the 2,723 cases, or in 140 cases. Of these, only 2 cases (both in females) occurred in the first decade of life (1.43 per cent), and 5 (4 in males and 1 in a female) occurred in the second decade (3.57 per cent). Thus a total of 5 per cent of the cases of calcification of the choroid plexus occurred within the first two decades of life, the period with which pediatricians are concerned. Figure 1 shows the distribution of the cases of calcification of the choroid plexus in this series according to age groups.

On the other hand, the number of children examined within the first decade was 176, so that the 2 cases of calcification of the choroid plexus observed actually represent a percentage incidence of 1.14 per cent within this age group. Since 370 patients were examined within the second decade, the 5 cases of calcification observed represent an incidence of 1.35 per cent within this second age group. Figure 2 is a graphic representation of the percentage incidence of this condition according to decades.

SITE AND CHARACTER OF CALCIFICATION

Whenever calcification occurs in the choroid plexus, it practically always is seen in the glomus, and, according to Dyke and Davidoff,[4] it is almost invariably bilateral. Normally the choroid plexus is not demonstrable in ordinary roentgenograms of the skull. It can be seen only in cases in which a sufficient amount of calcium has been deposited to cast a shadow. In Dyke's [2] series it was demonstrable in 5.1 per cent of the 2,723 roentgenograms of the skull, or in one twentieth of the cases in which plain roentgenograms were made.

5. Schüller, A.: Roentgendiagnostik der Gehirnkrankheiten: Die allgemeine Chirurgie der Gehirnkrankheiten, in von Bruns, P.: Neue deutsche Chirurgie Stuttgart, Ferdinand Enke, 1914, vol. 2, p. 343.

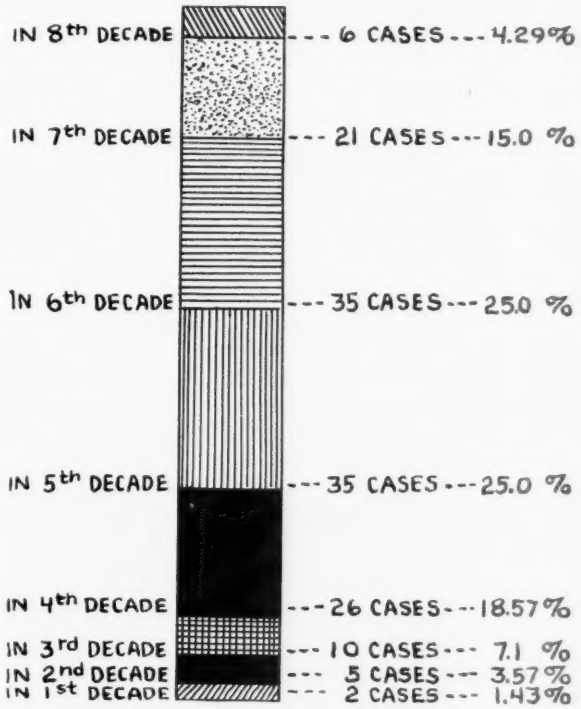
IN 8th DECADE --- 6 CASES --- 4.29%
IN 7th DECADE --- 21 CASES --- 15.0 %
IN 6th DECADE --- 35 CASES --- 25.0 %
IN 5th DECADE --- 35 CASES --- 25.0 %
IN 4th DECADE --- 26 CASES --- 18.57%
IN 3rd DECADE --- 10 CASES --- 7.1 %
IN 2nd DECADE --- 5 CASES --- 3.57%
IN 1st DECADE --- 2 CASES --- 1.43%

Fig. 1.—Distribution according to age groups of the 140 cases of calcification of the choroid plexus, observed roentgenographically. The total number of patients examined was 2,723. (Adapted from Dyke.)

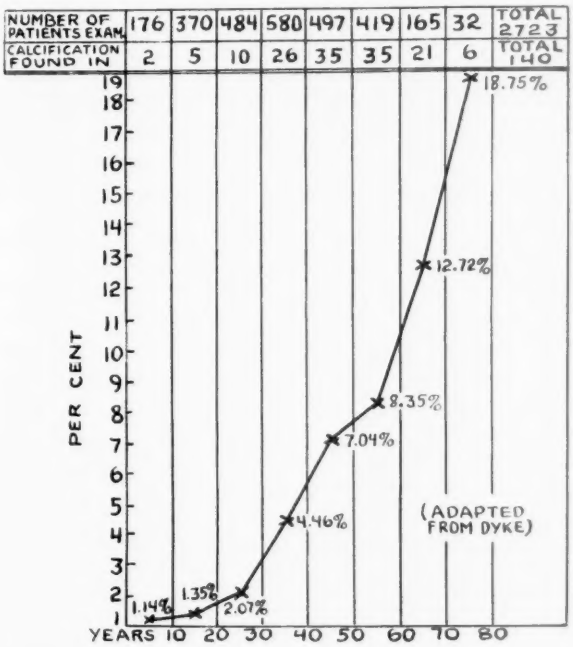

Fig. 2.—Percentage of incidence of calcification of the choroid plexus on routine roentgenographic examination of the skull according to decades (for each age group).

The deposits of calcium in the choroid plexus may be identified in the roentgenogram by the site and characteristics of the shadow. The glomus in each lateral ventricle is located about 2.5 cm. lateral to the midline on the anteroposterior film. On lateral views, the center of the calcified area is about 1 cm. behind and 0.5 cm. above the pineal shadow.

The deposit of calcium salts usually has a fairly characteristic appearance. The shadow may be very faint and barely perceptible if the calcium is scanty in amount. When calcium is present in small amounts, the shadow has a more or less circular form. It is seen as a cluster of dots, each about 2 mm. in diameter. Dyke and Davidoff [4] likened the appearance of this cluster of dots to a "popped kernel of corn" and stated that they may reach a size of 1 cm. or more. According to these authors, when calcification extends anteriorly in the choroid plexuses into the body or temporal horns of the lateral ventricles the shadows may take on a crescentic shape.

The fact that these shadows seen in the roentgenogram are really due to deposits of calcium in the choroid plexus has been definitely proved by Heuer and Dandy [1] and by Beals.[3] In a footnote on page 316 of their report, Heuer and Dandy stated that in their second case extensive calcification of the choroid plexus was noted at autopsy and that by postmortem studies the shadow in the roentgenograms was identified with this structure. Beal reported an instance in which characteristic shadows were seen in roentgenograms of the skull of a 39 year old patient during life, and at autopsy both gross and microscopic examination showed calcium in the glomuses of the choroid plexuses. He also had roentgenograms taken of the brain after the removal of the choroid plexuses, which failed to show the shadows seen prior to the extirpation. Thus in Beal's case the nature of the shadow seen in the roentgenograms was identified beyond any possible doubt as due to calcification of the choroid plexuses.

The next forward step was that of Dyke and Davidoff,[4] who by encephalographic studies were able to determine the position of the calcium deposits in the choroid plexuses relative to the ventricles after the latter had been rendered visible by the intraspinal injection of air. The calcified masses representing the choroid plexuses were found to have caused filling defects in the smooth outline of the ventricle in the encephalograms in several cases in which plain roentgenograms had shown calcification of the choroid plexuses. The size of the filling defect corresponded to that of the glomus in any given case. These investigators also noted a notch corresponding in size, shape and position to the defect produced by calcification of the choroid plexus in a number of encephalograms in cases in which plain roentgenograms of the skull had failed to show calcification. The notch or defect in the latter group of

roentgenograms has been ascribed by these investigators to the glomus of the choroid plexus. In a review of a series of 50 encephalograms with this point in mind, the filling defect was noted in one or both lateral ventricles in 23 instances, or in 46 per cent of the cases.

Thus Dyke and Davidoff have shown by encephalographic studies that the calcified glomus, visualized by a shadow in the plain roentgenogram, interferes with the filling of the ventricle with air in carrying out encephalography. An uncalcified glomus will cause a similar defect or notch but is demonstrable only in the encephalogram, since a shadow will not be seen on the plain roentgenogram owing to the absence of deposits of calcium.

SIGNIFICANCE

Apparently the presence of the deposits of calcium in the choroid plexus is not of pathologic significance. The presence of defects in the ventricles in encephalograms, whether they are the shadows of a calcium deposit or not, depends on the size of the choroid plexus and does not appear to be associated with any particular disease. Dyke and Davidoff [4] studied the encephalograms in a series of 50 cases of convulsive seizures, either primary or symptomatic. In 23 instances a notch or filling defect was observed in the ventricular outline of the bodies of the lateral ventricles or the roof of the fourth ventricle as outlined by air; in the other 27 instances no notch was demonstrated. When the clinical diagnoses in both these groups were reviewed, the same number of patients with epilepsy (9) was found in each. The authors concluded that the defects were of no pathologic significance but were to be found in a perfectly normal ventricular system and that their presence must not be misinterpreted as being due to a deformity of the ventricles by tumor or other cranial disease.

REPORT OF CASE

A. LaP., a 4 year old girl, was admitted to the Lenox Hill Hospital because of backward physical and mental development. She was born at full term and was delivered normally, weighing 8 pounds (3,628 Gm.). There was no cyanosis or other evidence of injury at birth. Dentition began at 6 months and was normal. The child did not hold her head up until she was 1 year of age. She sat up at 15 months and began to walk at 24 months but was always awkward. Articulation of a few words began at 24 months and had not improved prior to her admission to the hospital. She had never been ill save for occasional colds and for an umbilical hernioplasty done at 9 months of age. Two older sisters have rheumatic heart disease; the family history was otherwise irrelevant.

Physical examination revealed a somewhat obese 4 year old child with no abnormal findings save for the scar of the former umbilical hernioplasty. Her weight was 37 pounds (16.8 Kg.) and her height, 37 inches (93.9 cm.). She smiled constantly without cause and did not seem to understand or respond when addressed. A diagnosis of mental deficiency of unknown etiology was made.

The basal metabolic rate was plus 4 per cent. Urinalysis did not reveal any abnormal findings. The Wassermann test was negative with both antigens. Blood

chemical studies revealed normal values with calcium and phosphorus concentrations of 10.7 and 4 mg. per hundred cubic centimeters of serum, respectively. Pirquet and Mantoux tests with 0.1 and 0.5 mg. were negative.

Examination of the eyegrounds did not reveal any evidences of increased intracranial pressure or of retinal disturbances. To rule out further a possible intracranial cause for the apparently retarded mental development, a roentgenographic examination was made, but no evidence of increased intracranial pressure was found. However, on stereoscopic examination two definite shadows were observed which were interpreted as bilateral deposits of calcium (fig. 3). Roentgenographic examination of the upper and lower extremities was made to rule out calcinosis universalis, but no other deposits of calcium were found.

The actual diagnosis was unsuspected until the films were shown to Dr. L. M. Davidoff, who pointed out that the picture was typical of the calcification of the

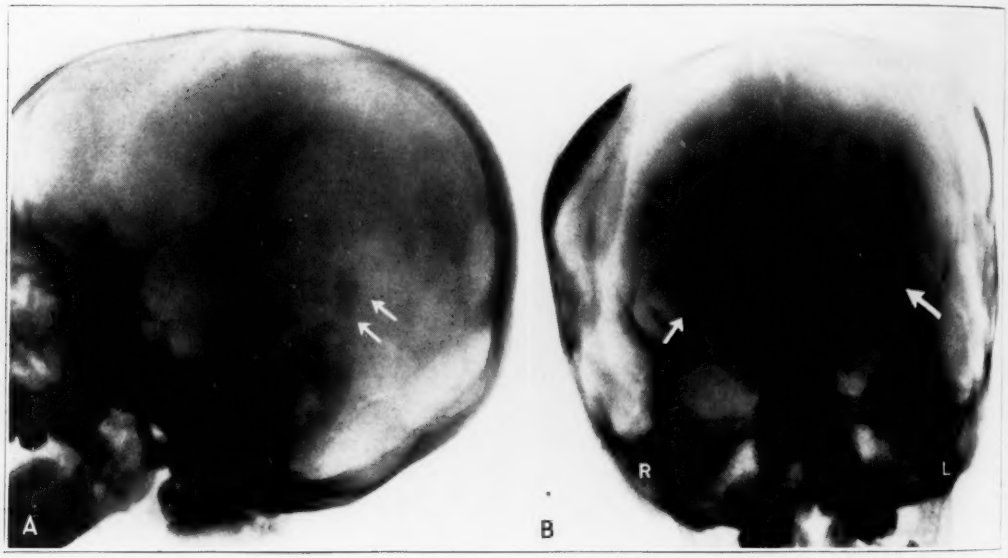

Fig. 3.—*A*, lateral view of the skull (plain film) showing calcification in the glomuses of the choroid plexus. Owing to a slight rotation of the head, the two glomuses are not superimposed but are seen as separate shadows. *B*, anteroposterior view of the skull (plain film) showing the calcified glomuses as two symmetrically placed shadows.

glomus of the choroid plexus reported in a series of cases in adults by Dr. Dyke and himself. He advised encephalographic studies to localize the shadows in their relation to the lateral ventricles.

Under general anesthesia, a lumbar puncture was done and air injected by Dr. I. P. Sobel according to the method outlined for encephalography by Davidoff and Dyke.[6] After 55 cc. of spinal fluid had been removed and 45 cc. of air had been injected, the ventricles were found to be properly visualized on the roentgenogram (plates having been taken at varying intervals during the procedure). The child did not suffer any ill effects save for a slight headache, which

6. Davidoff, L. M., and Dyke, C. G.: An Improved Method of Encephalography, Bull. Neurol. Inst. New York **2**:75, 1932.

persisted for several days. Her pulse and respiration were normal. Her color remained good. She was discharged in good condition a week afterward.

The encephalograms revealed filling of the ventricles in a normal manner. There was no recognizable cortical atrophy. The calcified areas were demonstrated at the site of the glomus of the choroid plexus causing a filling defect or notch in the smooth outline of the ventricle which was filled with air (fig. 4).

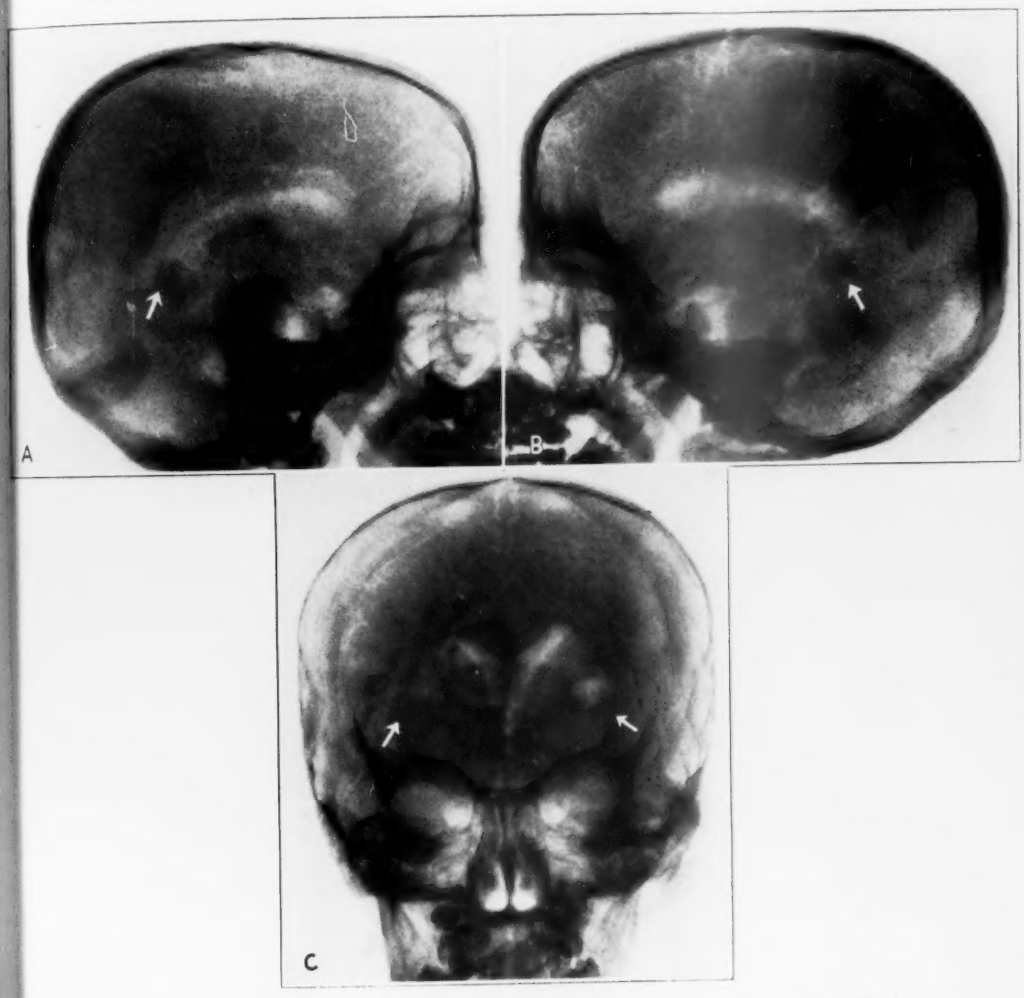

Fig. 4.—*A*, encephalogram (right lateral view illustrating the relation of the calcified glomus to the body of the ventricle. *B*, encephalogram (left lateral view). *C*, encephalogram (anteroposterior view) demonstrating the relation of the calcified glomus to the ventricle on each side.

The child was seen again five months later in the follow-up clinic. A marked improvement was evident, for the child walked well, spoke in phrases and partial sentences and answered questions intelligently. Her entire appearance seemed much more normal than before.

COMMENT

The case described herein is the only report of the calcification of the choroid plexus during childhood in the pediatric literature. Even in Dyke's paper [2] only the bare statement appears of the facts that two cases occurred in the first decade of life and five in the second decade, but no description of the cases was given, for his paper dealt with the larger consideration of the indirect signs of tumor of the brain as noted on routine roentgenographic examination of the skull.

In a careful survey of the literature, the only other published case report found is that by Strandquist.[7] The patient was a 5 year old boy with epilepsy; similar intracranial shadows of calcium deposits were seen in a plain roentgenogram of the skull. Unfortunately, no encephalographic studies were made, and the roentgenogram was not reproduced in the report.

The recognition and proper interpretation of these shadows seen in the plain roentgenogram and of the defect in the ventricular outline, as visualized in the encephalogram, are of utmost importance. Otherwise, a mistaken diagnosis of a pathologic intracranial lesion as, for instance, a tumor of the brain might be made. Since the finding of calcification seems to have no direct bearing on the clinical diagnosis, according to our present knowledge, it may be regarded as a normal finding.

Whether or not the introduction of air during encephalography caused the improvement in the clinical picture noted five months later in the case described herein cannot be determined. It is barely possible that some slight adhesions may have been broken by the introduction of air. However, it is more probable that the improvement was the natural result of normal growth and development, and its following so closely on the encephalographic examination would be merely coincidental.

CONCLUSION

A case of calcification of the choroid plexus in a 4 year old child is reported. The deposits of calcium were first observed in a plain roentgenogram of the skull. Subsequent encephalographic studies revealed the site to be the glomus of the choroid plexus and showed its relation to the ventricle.

The presence of deposits of calcium in the choroid plexus seems to have no obvious bearing on the clinical diagnosis. It is considered as a normal finding and at the present time does not seem to have any pathologic significance.

1085 Park Avenue.

7. Strandquist, B.: Fall av epilepsi med intrakranielle förkalkningar, Svenska Läk.-tidning. **30**:14, 1933.

Progress in Pediatrics

WILLIAM WADD
1776-1829

NURSERY MEMS AND ANECDOTAL BIOGRAPHIES

ARTHUR F. ABT, M.D.
CHICAGO

In the course of the centuries many pamphlets have been written on the care and diets of infants and children. John Ruhräh, in "Pediatrics of the Past," collected the works of many of the earlier essayists on this subject. He stated that Bartholomäus Metlinger in the fifteenth century, in his "Ein Regiment der jungen Kinder," included in his first chapters on general rules for the new-born and care of the infant during the early period of life much of the advice for care which is to be found in modern pamphlets on infant welfare. Felix Wurtz was a physician of the sixteenth century. In his "Children's Book" he outlined procedures for the care of children, how to bathe them and what to do for cramps, and he also added some notes on how to feed a small infant or child. These notes agree with modern teachings. The seventeenth century pediatricians gave more attention to the description of disease and therapeutics than to the general management and care of the infant. In the eighteenth century William Cadogan, in his essay "Nursing, and the Management of Children from Their Birth to Three Years of Age" devoted himself to precise detailed accounts of how to dress, clothe, bathe and care for infants and children and also of the type of diet and method of feeding best suited for them. George Armstrong, also an eighteenth century physician, appended an essay on nursing to his "Account of the Diseases Most Incident to Children," in which he gave sound advice as to the care and diet of the young infant.

William Wadd belongs to the latter part of the eighteenth century and the early part of the nineteenth. He was born on June 21, 1776. He was the eldest son of Solomon Wadd, a London surgeon (fig. 1). In 1784 he attended the Merchant Taylor's School, and in 1797 he was apprenticed as a pupil of James Earle, a surgeon at St. Bartholomew's Hospital. In 1801 he was admitted to membership in the Royal College of Surgeons. In 1824 he was chosen a member of the Council of the College of Surgeons of England. He was appointed as Surgeon-Extraordinary to the Prince Regent in 1817, and as Surgeon Extraordinary to King George IV in 1821. In 1829 he was appointed a member of the Court of Examiners of the College of Surgeons of England

to succeed John Abernathy. On Aug. 29, 1829, while making a holiday tour in Ireland he met his death when he jumped from a runaway car in a road leading from Killarney.

Wadd was the author of a number of treatises and was a man of great wit as can be deduced from the anecdotes which are contained in his writings. He was also an artist of considerable talent and a proficient etcher. In fact, all of the illustrations in his various treatises are by his own hand. A life-size painting of Wadd in oils

Fig. 1.—A portrait of Solomon Wadd, the London surgeon, by his son William Wadd. It is reproduced from an original etching at the Northwestern University Medical School from the private collection of Dr. Irving Cutter.

by John Jackson is said to hang in the Secretary's office at the Royal College of Surgeons in Lincoln's Inn Fields.

According to D'Arcy Power,[1] Wadd was the author of:

1. "Practical Observations on Strictures," London, 1809, 8vo; 2nd ed. 1811; reissued 1812; 3rd ed. 1826. 2. "Cursory Remarks on Corpulence," London, 1810.

1. Dictionary of National Biography, London, Smith, Elder & Co., 1899, vol. 58, p. 405.

8 vo., issued anonymously; 3rd ed. 1816; reissued in an enlarged form as "Comments on Corpulency, Lineaments of Leanness, Mems on Diet and Dietetics," London, 1829, 8 vo. The etchings in this volume remind one of Cruikshank. 3. "Cases of Diseased Bladder and Testicle," London, 1815, 4 to, with twenty-one plates; reissued 1814; 4. "Cases of Diseased Prepuce and Scrotum," London, 1817, 4 to, with twelve plates. 5. "On Malformations and Diseases of the Head," London, 1819, 4 to, with eleven plates. 6. "Illustrations of Morbid Anatomy," London, 1824, fol. with seventy-eight plates. The original drawings are in the Royal College of Surgeons of England. There is no letterpress attached to the work beyond the title-page. 7. "Nugae Chirurgicae, or a Biographical Miscellany Illustrative of a Collection of Professional Portraits," London, 1824, 8 vo. This is the work by which Wadd's name is best known. The nucleus of the collection of portraits was presented to him about 1814 by Henry Fauntleroy, the banker who was hanged for forgery. The catalogue is arranged under two alphabets—one of anecdotal biographies, the other of memorabilia. The work is excellent reading, but it is full of inaccuracies both of dates and names. 8. "Nugae Canorae, or Epitaphian Mementoes (in stone-cutters' verse), of the Medici Family, by Unus Quorum," London, 1827, 8 vo. 9. "Mems, Maxims, and Memoirs," London, 1827, 8 vo. Both volumes contain a miscellany of things medical, and of the history of medicine and surgery in England. Many have utilized them, but few have acknowledged their indebtedness. They show a wide reading, but are thoroughly uncritical.

Wadd's "Nugae Chirurgicae" and his "Mems, Maxims, and Memoirs" cannot be considered accurate sources for historical medical facts. He makes only brief and cryptic mention of the greater medical personages whom he includes in his biographies. For example:

> Erasmus Darwin, M.D. F.R.S.—S. J. Arnold pinx. B. Pym sc. 1801.
> Born 1731—Died 1802.
> Onward he steps, Disease and Death retire,
> And murmuring Demons hate him and admire.
>
> Botanic Garden, Cant. ii.—Gent. Mag. Nichol's Lit. Anec. vol. IX.

William Harvey—Physician to Charles I. Houbraken Sc. The discoverer of the circulation. Died 1657. He was buried at Hempstead in Essex, not at Hemel Hempsted, as stated in some accounts of his life.

Hippocrates.—Bovi sc. Hippocrates may be considered the first who had any fair pretensions to the character of a Surgeon. Besides medical, he expressly treated on surgical subjects, and performed operations, though, for reasons known only to himself, he did not choose to perform the operation of Lithotomy.

Edward Jenner, M.D. F.R.S.—J. Hazlitt pinx. C. Turner sc., 1808. Died 1822. Gent. Mag.

Thomas Linacre, M.D.—Born 1460—Died 1524. Founder of the College of Physicians and first President—Hutchinson.

Morgagni—The celebrated Anatomist.

Ambrose Paré—Fiquel Sc. Died 1590—A celebrated French Surgeon to Henry II. Francis II. Charles IX. and Henry III.

Sydenham, Thomas, M.D.—Born 1624. The most eminent Physician and improver of art that England has produced.

These biographies do, however, contain many gems of anecdotal wit. A few excerpts may be quoted. In "Nugae Chirurgicae" he notes the following anecdote concerning William Battie:

A fair opening for a Physician happening at Uxbridge, induced him to settle in that quarter. At his first coming there, the Provost of Eton, Dr. Godolphin, sent his coach and four for him, as his patient; but the Doctor sitting down to write a prescription, the Provost, raising up himself, said, "You need not trouble yourself to write; I only sent for you to give you some credit in the neighborhood."

Wadd's note on Thomas Brown is as follows:

Author of Religio Medici, a paradoxical book, translated into almost every language in Europe. This learned person was of opinion, that love was a folly beneath a philosopher; and says, he "could be content that we might procreate like trees, without conjunction." He descended, however, from his philosophic dignity, and married an agreeable woman. His reason for marrying was, "because he could discover no better method of procreation."

The question of medical fees was no doubt a lively topic of conversation whenever medical practitioners got together in Wadd's day just as it is in our time. He has the following to say about Euricus Cordus:

Cordus, who was accustomed to receive his fees only at the termination of his patients' disease, describes, in a facetious epigram, the practitioner at three different times, in three different characters.

"Tres medicus facies habet; unam, quando rogatur,
Angelicam; mox est, cum juvat, ipse Deus.
Post ubi curato, poscit sua praemia, morbo,
Horridus apparet, terribilisque Sathan."

"Three faces wears the doctor; when first sought
An angel's—and a god's the cure half wrought:
But, when that cure complete, he seeks his fee,
The devil looks less terrible than he."

He gives the following anecdote about Thomas Dawson:

After he became M.D. he attended his neighbour Miss Corbett, of Hackney, who was indisposed; and found her one day sitting solitary, piously and pensively musing upon the Bible, when, *by some strange accident,* his eyes were directed to the passage where Nathan says to David: "Thou are the Man." The Doctor profited by the kind hint; and, after a proper time allowed for drawing up articles of capitulation, the lady, on 29 May, 1758, surrendered herself up to all his prescriptions, and the Doctor very speedily performed a perfect cure.

The portrait of Robert Glynn inspired Wadd to make the following comment:

He studied Medicine, but preferred the indolent life of a College to practice. After being 63 years, for his wit, his learning, and his interesting fund of anecdotes, the favourite of his society, he died 1800, aged 82. He is known as the author of the "Day of Judgment," a poem of merit, which obtained the Setonian

prize at Cambridge 1757. His portrait, and the following *jeu d'esprit*, prove his physiognomy not to have been of so agreeable a cast.

"This morning, quite dead, Tom was found in his bed.
Altho' he was hearty last night;
But 'tis thought, having seen Dr. Glynn in a dream,
That the poor fellow died of the fright."

According to Wadd's comment on Daniel Kenrick, some of the early members of the profession were also devotees of the favorite pastime of Isaac Walton. He has this to say of Kenrick's ability as a fisherman:

Dr. Kenrick practised as a Physician at Worcester. He was not a graduate, nor very able in his profession; but was esteemed a man of wit, and a jolly companion. These lines, "Upon a Giant Angling," printed in the fifth volume of Dryden's "Miscellany," are said to have been written by him:

"His angle-rod made of a sturdy oak,
His line a cable that in storms ne'er broke,
His hook he baited with a dragon's tail,
And sat upon a rock and bob'd for whale."

The portrait of Julius Caesar Scaliger caused Wadd to feel that the vain and pompous were not all of his generation:

The two Scaligers, father and son, were prodigies of learning and vanity. Joseph Scaliger inherited from his father the most ardent love for study, the most ridiculous vanity, with a most caustic humor. His writings are a mass of useful materials and gross invectives. He was a literary despot. In 1594 he published a work on "The Antiquity and Splendour of the Scaligerian Race," and he makes his father to be the greatest warrior, the most skilful Physician, and the best Latinist of the age. This flaming account was refuted by Scioppius, who made a calculation of the number of lies it contained, which he informs us amounted to 499.

Wadd's description of the death of John Belchier is as follows:

He was a very stout, heavy man, a few hours before he died he fell on the floor, when his man servant, not being able to raise him, offered to go for help, he said, "no, John, I am dying, fetch me a pillow, I may as well die here as any where else"; and very shortly expired.

Wadd quotes a very personal polemic in verse between George Cheyne and a Doctor Wynter:

A North Briton, and a Physician, who enforced the doctrines he taught, by his personal example. This conduct created a host of enemies, who attacked, but never defeated, their intrepid antagonist. The following "jeux d'esprits," though often related, prove this assertion.

Dr. Wynter to Dr. Cheyne

"Tell me from whom, fat-headed Scot,
Thou didst thy system learn;
From Hippocrates thou hadst it not,
Nor Celsus, nor Pitcairn.

"Suppose we own that milk is good,
And say the same of grass;
The one for babes is only food,
The other for an ass.

"Doctor! one new prescription try,
(A friend's advice forgive),
Eat grass, reduce thyself, and die,
Thy patients then may live."

Dr. Cheyne to Dr. Wynter

"My system, Doctor, is my own;
No tutor I pretend:
My blunders hurt myself alone,
But yours your dearest friend.

"Were you to milk and straw confin'd
Thrice happy might you be;
Perhaps you might regain your mind,
And from your wit be free.

"I can't your kind prescription try,
But heartily forgive;
'Tis nat'ral you should wish me die
That you yourself may live."

Evidently Wadd had no great use for a teetotaler. This may be deduced from his comments on Philemon Holland:

The "Translator General of his Age" continued to translate till he was 80 years old; and it is surprising, considering that he united the professions of Schoolmaster and Doctor, that he could find time to translate so much, a single pen producing a large folio! His literary feats, however, were greatly exceeded by Andrew Tiraqueau, who is said to have produced a book and a child every year, till there were twenty of each, or as some say thirty. This, with the circumstance of his being a water-drinker, occasioned the following jocular epitaph:

"Hic Jacet, qui aquam bibendo viginti liberos suscepit viginti libros edidit. Si merum bibisset, totum orbem implevisset."
"Here lies a man who, drinking only water,
Wrote twenty books, with each had son or daughter;
Had he but used the juice of generous vats,
The world would scarce have held his books and brats."

In his memoirs on John Hunter, Wadd relates the following anecdotes:

In former times it would appear as if some operations were done for the patient, and some for the practitioner. A friend of mine met a sailor with a wooden leg, "his precious limb was lopped off,"—"And where was it lopped off?"—"At St. Thomas's,"—"And what was it lopped off for?"—"Why as to the matter o' that," quoth Jack, "nothing, that I could ever see." Mr. Hunter, who did more than any human being, to lessen the frequency of operations, once had a patient of a similar kind. He was a most anxious man about an operation, which, in those days, were attended almost with the formalities of an execution. He had got on *his dress*, and a profound silence reigned in the theatre;—the surgery-

man was ordered to bring in the patient who was to have his leg taken off. The surgery-man disappeared; in two minutes he returned with a face as long as the leg, solus—"Why do you not bring in the patient?" was demanded by the expectant operator,—"Because Sir," said the astonished surgery-man, "Because, Sir, he has ran-away."

An etching which illustrates Wadd's ability at caricature appears in "Mems, Maxims, and Memoirs" depicting the peculiar costume which he says physicians wore in certain countries (fig. 2).

Fig. 2.—A reproduction of an engraving of an etching by Wadd of the peculiar costume which he states physicians were ordered to wear in certain countries. From "Mems, Maxims and Memoirs," 1827.

Wadd's pamphlet "Comments on Corpulency, Lineaments of Leanness, Mems on Diets and Dietetics," also contains his "nursery mems." On the title-page is a device which is apparently of Wadd's own construction. Leonard Williams [2] stated that the references in this device which appears on the title-page are not all quite clear (fig. 3).

2. Williams, Leonard: Obesity, New York, Oxford University Press, 1926.

Apicius.—M. Gabius Apicius flourished under Tiberius. After squandering upwards of 800,000 pounds upon his stomach, he found that little more than 80,000 pounds remained; upon which, despairing of being able to satisfy the cravings of hunger from such a pittance, he forthwith hanged himself. But he was not forgotten. Sundry cakes (Apicia) and sauces long kept alive his memory;

COMMENTS ON CORPULENCY

LINEAMENTS OF LEANNESS

MEMS ON

DIET AND DIETETICS.

By WILLIAM WADD, Esq. F.L.S.

Surgeon Extraordinary to the King,

etc. etc. etc.

LONDON:

JOHN EBERS & Co., OLD BOND STREET.

MDCCCXXIX.

Fig. 3.—The title-page to "Comments on Corpulency," 1829, bearing a device of Wadd's own construction, which is explained in the text.

Apion, the grammarian, composed a work upon his luxurious labours, and his name passed into a proverb in all matters connected with the pleasures of the table.

Ude.—On the first page of advertisements at the end of Wadd's book there are set forth the particulars of a work called The French Cook, by Louis Eustach Ude, ci-devant cook to Louis XVI and the Earl of Sefton, "Now Maitre d'Hotel at Crockford Club, St. James's Street."

Lewis Carnaro.—A Venetian, mentioned in the text as advocating that every mouthful of food be masticated until it becomes fluid and tasteless. He wrote a book, Trattato della vita sobria, which has been described as the best treatise in any language on personal hygiene and the simple life. He lived to be nearly one hundred (1467-1566) and published his book when he was ninety-one.

Heliogabalus or Elagabalus, Roman Emperor, A. D. 218-222.—The reign of this prince, who perished at eighteen, was characterised by the most fantastic folly and superstition, together with impurity so bestial that the particulars almost transcend the limits of credibility. The curved rod is the augur's litmus. The

Fig. 4.—The frontispiece to "Comments on Corpulency," 1829, signed by Wadd.

letters S. C. signify Senatus Consulto, but the significance of the stork is a mystery. Mr. G. F. Barwick, of the British Museum, who kindly took considerable trouble to elucidate the meaning of the device in general, and the meaning of the stork in particular, writes that the bird never occurs on Roman or Greek coins, but only on gems. He then proceeds as follows:

"On looking up the history of Heliogabalus (Elagabalus), I find that he gained the purple by the statement that he was the son of Caracalla by Soemius, and not of his reputed father, Varius Marcellus. On becoming Emperer, he summoned his mother to the Senate (the only instance of a woman in history) and made her a 'testis' with the Consuls to the 'Senatus Consulta.' Now the legend

of the stork is that it nourishes its young and fosters them, and in return the young feed the parent bird, so I suggest that the stork represents Heliogabalus as a type of filial piety in return for maternal solicitude.

"The L. A. S. (under the word 'Ude') may possibly be L. S., with a pointed ornament in the middle to stand for 'locus sigilli,' with a wax impression embedding the tie of the 'bullae' of Cornoro. This is perhaps rather vague, for the Cornoro medal seems to be attached by a soldered ring. Is it possibly the L. A. Sc. of Schola Salernitana? This seems to me far more probable."

Fig. 5.—The illustration opposite page 55 in "Comments on Corpulency," signed by Wadd. It represents an engraving of an etching by him.

Wadd's "Comments on Corpulency" contains gems of wit which must be read in entirety to be fully appreciated. The treatise is as appropriate today as when it was written one hundred years ago. The work is beautifully illustrated by numerous etchings signed by Wadd. A few examples will illustrate the skill and talent as an etcher which he possessed (figs. 4, 5, 6 and 7). Leonard Williams has quoted many excerpts from Wadd in his recent book on "Obesity."

It is the "nursery mems" with which we are most particularly concerned. These begin as follows:

Formerly, all the rules and regulations of life, particularly nursery regulations, were drawn from the "Domestic Medicine." With some, "Buchan" was next to the Bible. These were facetiously denominated "Buchaneers." "Buchan, Sir, has done more towards improving the health and shape of our girls, than any man living," said one old lady; "he popped them all into cold water at Christmas." "But for Buchan, my poor husband would have died ten years sooner than he

Fig. 6.—The illustration opposite page 75 in "Comments on Corpulency," signed by Wadd, illustrating obesity in the fair sex. Wadd states: "The annexed sketch is of a woman whose petticoat would have fitted Falstaff, as well as that of the fat woman of Brentford."

did," rejoined a young widow. "Ah! he was a fine man!" echoed a third. Buchan, however, died one day, and with him were buried many of the plans by which some people had been braced into health, and others braced out of the world. The late Margravine of Anspach, was, at an early period of her life, so reduced by weakness, that a sister only two years older than herself, actually carried her about in her arms; to give her strength, cold bathing was ordered, which produced an ague, from which she with difficulty recovered.

We have heard the case described of a poor infant, who was preposterously dipped every morning into iced water. The dread of the little creature, as she was carried towards the scene of her suffering, was most tragically evinced, by her violent trembling, and clinging to her nurse, for she was not old enough to speak; but when she was held over the bath, preparatory to the remorseless plunge, her limbs became almost convulsed, and her soft and baby face, which one might imagine incapable of any expression, was momentarily visited with a premature character, in the deformity of its terror; and the beseeching looks

Fig. 7.—Wadd's illustration of leanness. The greyhound is appropriately added for comparison.

cast toward her father, who yielding to injudicious advice, used to sanction the operation. The child died of hydrocephalus.

The barbarous practice of hardening children, then went out of fashion. Our ears are no longer assailed, with the convulsive screams of half-drowned children, whose worthy parents believed they were sacrificing themselves, for the good of their offspring. What stuff have we not heard about "inuring children to hardiness." These excellent people forgot to confer the Spartan constitution, before they introduced the Spartan discipline; yet, against the experience of common sense, and the convulsive screams of baby eloquence, they confidently hoped to

turn nature from her course. Who would have ventured to oppose the sacrifice of such amiable feelings? Who could have uncourteously hinted, that the sudden chilling of the skin repels capillary action and thereby increases the vascular action of internal parts?

The custom of hardening infants and children seems to crop up perennially. How often today could one quote Wadd's exact words to some young mother!

This system, however, was succeeded by another equally pernicious. It might be called the "Coddling System;" and children, instead of being braced, were stuffed to death. The disorders of children, were discovered to arise from wind. Wind was the effect of emptiness, consequently the more they cried, the more they were stuffed: "Godfrey's Cordial," "Dalby's Carminative," and thick pap, being administered in proportion: the nurse, like a skilful pilot, steering according to the way the "wind blew."

Even today we have with us mothers and nurses who, like the good sailorman that Wadd describes, steer their baby's diet according to the way the wind blows: Who has not had to contend with such a one, who varied her course between a purge and camomile tea? Wadd continues:

This system, like the other, had its day, till good sense, and good nature overcame it. But if we have got rid of some of these prejudices, are we still, in our enlightened times, exempt from error? Have we not very learned ladies now-a-days, whose "Domestic Medicine" is equally potent? Woe be to the child with a hot head, if his mother has ever heard of "Hydrocephalus acutus." Woe be to "papa's darling," if mamma understands the administration of calomel! "Doctor," said a lady to Reynolds one day, "I have sent for you because we cannot get on with this child; we have given five grains of calomel, and repeated the dose, but all without success!" The child was in a state which medical men will understand; and which extorted from the Doctor the emphatic exclamation, "Calomel will soon be measured by the spoonful!" Within these few days, a gentleman, whose excellent lady is skilled in Domestic Medicine, in answer to the question, "How d'ye do?" replied "I am very well, only a little over calomelized!" Strange! that one who would not dream of understanding the machinery of a watch, would think the complicated machinery of the human frame, more easily comprehended!

Mr. Brande, in some very sensible remarks on this subject, uses a very appropriate epithet. He calls it domestic empiricism! "At a time," he says, "when domestic empiricism is so prevalent, as at present, it is important to point out the dangers which may arise from the uses, or rather abuses of the most simple remedies.

"Every medical practitioner must have repeatedly witnessed the serious and sometimes fatal consequences, attendant upon the imprudent use of the stronger medicines, which are so extensively supplied for family consumption, particularly preparations of antimony, mercury and opium; which, under a great variety of seducing forms and titles, are constantly employed; they are not, however, aware of the prejudicial effects of magnesia." He then proceeds to state the case of a lady, who, in the course of two years and a half, took from nine to ten pounds of

weight of magnesia; and notice another, in which from four to six pounds of insoluble magnesia were found in the colon of a deceased nobleman.

The great science that watches over health, is as complicated, as it is important. It requires attainments of the highest order—knowledge of every kind—and after the experience of ages, still remains, to the most learned and most skilful, "a conjectural art." While private quackery, like public quackery, being founded in ignorance, and having nothing to conjecture—has nothing to fear.

Wadd's remarks on self-medication and the advice offered by the neighbor lady across the hall are as true today as when they were written. Nearly every practitioner meets with such occurrences on his daily round. Perhaps for one who returns to his fireside of an evening sorely irked by the foibles and follies of the guardians of his youthful patients the perusal of William Wadd's humorous and quaint recital of similar experiences in his day may prove cheering and refreshing as a draught from a cool sparkling spring.

News and Comment

GENERAL

Physicians Certified by American Board of Pediatrics.—The following have been certified by the American Board of Pediatrics since the last report: George B. Bader, New York; Elmer Walter Barron, Boston; Tobias L. Birnberg, St. Paul; Robert E. Cummings, Chicago; Clarence F. Friedman, Brooklyn; Joseph Garland, Boston; Howard B. Hamilton, Omaha; Alfred Collard Henderson, Stamford, Conn.; Jerome L. Kohn, New York; Robert H. Kotte, Cincinnati; Julian M. Lyon, Ardmore, Pa.; Herman L. Maslow, Brooklyn; W. Ambrose McGee, Richmond, Va.; A. Lane Mitchell, Houston, Texas; Arthur Gardner Quinn, Memphis, Tenn.; John Porter Scott, Philadelphia; Norman Survis, New Rochelle, N. Y.; Donald Kendrick Woods, San Diego, Calif.; Harry S. Andrews, Louisville, Ky.; George Lamar Arrington, Meridian, Miss.; James Lewis Blanton, Fairmont, W. Va.; Harry H. Boyle, Chicago; James Bennett Gillespie, Urbana, Ill.; David William Goltman, Memphis, Tenn.; Edgar Alphonso Hines, Seneca, S. C.; Cecil Oliver Lorio, Baton Rouge, La.; Robert H. McCrackin, Elat, Africa; James Dallas McKinney, Champaign, Ill.; John Collins McKitterick, Burlington, Iowa; Herman Frederic Meyer, Chicago; Ben H. Nicholson, Oklahoma City; Lee Palmer, Louisville, Ky.; Harold D. Pyle, South Bend, Ind.; Warren Wilson Quillian, Coral Gables, Fla.; Heyworth Naylor Sanford, Chicago; Mary Burchard Spahr, Ithaca, N. Y.; Brick Pomeroy Storts, Tucson, Ariz.; Ernest Starr Watson, Elmhurst, Ill.; Walter Merrill Whitaker, Quincy, Ill.; Robert E. Williams, Chicago; Robert Ermon Wilson, Greenville, Miss.; Max Reagen Woodward, Sherman, Texas; Meldrum Keplinger Wylder, Albuquerque, N. M.

In this group twenty-five took the examination. At that examination, which was held in St. Louis, on Nov. 19 and 20, 1935, thirty-one took the examination, and six failed. Of the twenty-five who passed, four were in Group I, seven in Group II and fourteen in Group III. Of those who failed, none was in Group I; one was in Group II, and five were in Group III.

UNIVERSITY NEWS

Dr. Giovanni de Toni has been made director of the Pediatric Clinic of the Royal University of Modena, replacing Professor Simonini, who had reached the age limit.

DEATHS

Dr. Silber C. Peacock, a well known, young pediatrician of Chicago, was murdered while making a night call on Thursday, Jan. 2. Dr. Peacock had done some good work on immunization against scarlet fever, and his loss will be felt. He was a member of the staff of the Children's Memorial Hospital.

SOCIETY NEWS

American Orthopsychiatric Association.—The thirteenth annual meeting of the American Orthopsychiatric Association will be held at the Statler Hotel in Cleveland on Feb. 20, 21 and 22, 1936. Information may be obtained from Dr. George S. Stevenson, secretary, 50 West Fiftieth Street, New York.

Abstracts from Current Literature

Pathology, Bacteriology and Biochemistry

Reaction of the Anterior Pituitaries of Immature Female Rats to Injection of Pregnancy Urine Extracts. J. M. Wolfe, Am. J. Physiol. **110**: 159 (Nov.) 1934.

Thirty-one immature female rats (from 21 to 25 days old) received from 25 to 75 units of extract of pregnancy urine daily for from seven to fifteen days. Thirty-three litter-mate sisters served as controls. The ovaries of the animals that were given the injections were markedly increased in weight, while the pituitary bodies were moderately increased in weight. Histologically, the anterior lobes of the pituitary bodies of the rats given the injections exhibited a loss of granules from the eosinophils, which were also decreased in relative percentage. The most striking changes were found in the basophils, which were enlarged and exhibited marked loss of granules. They were reduced in percentage. The percentage of the chromophobes was increased. Mitoses were more abundant in the anterior lobes of the pituitary bodies of the rats given the injections.

Nourse, Cleveland.

Experimental Diabetes Insipidus: Its Relation to the Anterior and Posterior Lobes of the Hypophysis. Curt P. Richter, Am. J. Physiol. **110**: 439 (Dec.) 1934.

Total removal of the pituitary glands of rats produced temporary diabetes insipidus. Permanent diabetes insipidus was produced when the posterior lobe was entirely removed, with a part of the anterior lobe remaining. The degree of the permanent diabetes insipidus seems to depend on the amount of the anterior lobe remaining and whether or not this lobe is still in connection with the pituitary stalk.

Nourse, Cleveland.

Reduction of Thymus by Gonadotropic Hormone. H. M. Evans and M. E. Simpson, Anat. Rec. **60**:423, 1934.

The gonadotropic hormone of pregnant mares was injected into male and female rats over a period of time. It brought about atrophy of the thymus gland. If the testes or ovaries had been previously removed there was no effect on the thymus.

Snelling, Toronto, Canada.

A Thirty-Minute Spectrographic Micro-Method for the Detection of Pathological Lead in Peripheral Blood. Harold Blumberg and T. F. McNair Scott, Bull. Johns Hopkins Hosp. **56**:32 (Jan.) 1935.

A thirty minute spectrographic micromethod for the detection of pathologic amounts of lead in 0.1 cc. samples of peripheral blood is described. It is suggested that this rapid and convenient method may be a valuable aid in the diagnosis of lead poisoning.

Authors' Summary.

Researches on Tetanus: II. The Toxin of the Bacillus Tetani Is Not Transported to the Central Nervous System by Any Component of the Peripheral Nerve Trunks. John J. Abel, E. A. Evans Jr., B. Hampil and F. C. Lee, Bull. Johns Hopkins Hosp. **56**:84 (Feb.) 1935.

We have presented many considerations and many facts in support of our belief that tetanus toxin and dyestuffs injected in an aqueous medium either intra-

neurally, subcutaneously, intramuscularly or intravenously are not carried in the axis-cylinders, the lymphatic vessels or the tissue spaces of peripheral motor nerves to the reacting cells of the central nervous system. We have also cited the recent investigations of anatomists who have traced the outflow of lymph from nerve trunks and have shown that it, like the lymph of other structures of the body, is added finally to the venous blood and not to the cerebrospinal fluid.

We furthermore called attention to a series of investigations that were carried out by Abel and Abel and Turner in 1910 to 1914, in which it was conclusively shown that alkaloids and dyestuffs cannot be distributed throughout the body by any peripheral mechanism, such as the "tissue spaces."

An account will be given in later papers of experiments that have been in progress in our laboratories for more than two years on the pathogeny of local tetanus, on the influence of complete denervation of muscles on the course of the poisoning and on the reflex phenomena and other aspects of both experimental and natural tetanus. We find ourselves as unable to accept the current theories in regard to many of these characteristics as we are to accept the theory of nerve transport, for the very good reason that this untenable theory is here also made to serve as the basis for their explanation.

AUTHORS' SUMMARY.

THE INTERRELATIONSHIP OF THE ADRENAL CORTEX AND THE ANTERIOR LOBE OF THE HYPOPHYSIS. H. B. SHUMACKER JR. and W. M. FIROR, Endocrinology **18**:676 (Nov.-Dec.) 1934.

After reviewing the literature concerning anatomic changes in the adrenal glands in hyperpituitarism and hypopituitarism. Shumack and Firor report a series of experiments on normal and hypophysectomized and adrenalectomized rats to demonstrate the effects of daily transplants of the pituitary body and of injections of cortical hormone, of ascorbic acid and of physiologic solution of sodium chloride. From these varied experiments they draw the following chief conclusions:

Both clinically and experimentally, severe pituitary deficiency causes a striking atrophy of the adrenal cortex, which may be restored to normal in animals by substitution therapy. Hyperpituitarism, conversely, results in a hyperplasia of the adrenal cortex. Hypophysectomy destroys the capacity of the adrenal gland to undergo compensatory hypertrophy if one gland is removed. Likewise, adrenal insufficiency results in anatomic changes in the hypophysis, the most characteristic of which is a diminution in the number of the normal basophilic cells.

Both pituitary and adrenal deprivation cause a stunting of growth, inactivity and lowered body temperature. Growth cannot be restored to hypophysectomized animals, activity increased, or temperature raised by potent extracts of adrenal cortical hormone. Loss of weight cannot be checked in adrenalectomized rats or growth stimulated by transplants of the pituitary gland.

In both adrenalectomized and hypophysectomized animals there are atrophy of the reproductive system and marked alteration in sexual activity.

Transplants of the pituitary body induce estrus in adrenalectomized rats and not only prevent ovarian atrophy but even stimulate excessive genital growth and premature sexual maturity. Implants of the pituitary body induce premature sexual maturity in adrenalectomized immature female rats.

JACOBSEN, Buffalo, N. Y.

CONTEMPLATING THE HORMONES. OSCAR RIDDLE, Endocrinology **19**:1 (Jan.-Feb.) 1935.

This paper is a review of recent significant advances in the field of endocrinology. Of particular interest to the pediatrician is the author's summary of new findings relative to the function of the thymus gland.

Twenty years ago Gudernatsch observed that at a particular phase of the tadpole's development the growth processes are specifically accelerated by feeding the animal thymus tissue. Ten years ago Riddle showed that the formation of egg-albumin and egg-shell in certain birds depends on a product of the thymus. Four years ago Asher showed that a substance obtained from the thymus had growth-promoting power in rats. Recent results obtained by Rowntree and Clark are most striking. In the fourth and fifth generation of rats given injections of extracts of thymus the teeth erupted in less than twenty-four hours after birth (this occurred within from nine to ten days in controls); the eyes opened on from the second to the third day instead of within from fourteen to seventeen days; the animals were covered with fur by the second or third day instead of within from fourteen to seventeen days as in controls. The young of the fifth generation were weaned when 2 or 3 days old and "at 6 days they could swim like muskrats and seemed as competent in water as in their cages." The time of adolescence was advanced to from the fourth to the eighteenth day, as compared to the normal time of from forty to ninety days. Fertility was increased.

These are new reasons for admitting the thymus into the family circle of busy hormones, and the new data are of such a nature that they will not fail to gain the attention of clinicians and biologists generally.

JACOBSEN, Buffalo, N. Y.

AIR STUDIES AT HIGHER ALTITUDES. E. L. MACQUIDDY, J. Allergy **6**:123 (Jan.) 1935.

The spore, bacteria and pollen content of the air surrounding Omaha at an altitude ranging from 3,000 to 5,000 feet (914.63 to 1,529.05 meters) was studied.

Pollen was found in large quantities at an elevation up to and including 3,000 feet during the pollinating season. Spores and bacteria were found in large quantities up to 3,000 feet, but in decreasing number above 4,000 feet (1,219.51 meters). The studies included an altitude of 7,000 feet (2,134.14 meters), where bacteria and spores were found.

Atmospheric conditions affected the counts.

HOYER, Cincinnati.

STAINING OF THE PROCESSES (FLAGELLA) OF HUMAN ERYTHROCYTES. WADE W. OLIVER, J. Infect. Dis. **55**:266 (Nov.-Dec.) 1934.

Oliver describes a method whereby the processes or flagella of normal red blood cells can be stained in smears.

TOOMEY, Cleveland.

DISSOCIATION OF THE GONOCOCCUS. CLARA RAVEN, J. Infect. Dis. **55**:328 (Nov.-Dec.) 1934.

To those who believe that the gonococcus is always gram-negative this article will be revealing. The author's summary is as follows:

"The typical form of the gonococcus may undergo dissociative changes which include pleomorphic forms, gram-positive diplococci, micrococci and beadlike bacilli; these dissociative changes are accompanied by alterations in the fermentation of sugars and by changes in serologic reactions. Dissociative forms may be reverted to the parent type. The changes described may be comparable to those occurring in the human body during the course of gonococcus infection."

A bibliography on the subject of dissociation may be obtained by consulting the literature quoted.

TOOMEY, Cleveland.

THE CULTURAL AND AGGLUTINATIVE RELATIONSHIPS OF INTESTINAL STREPTOCOCCI. JOHN C. TORREY and ELIZABETH MONTU, J. Infect. Dis. **55**:340 (Nov.-Dec.) 1934.

This article is of importance to pediatricians. Bargen, in 1924, described a diplostreptococcus which he thought was the specific etiologic factor in the pro-

duction of chronic ulcerative colitis. Torrey and Montu arrive at the following conclusions:

"No specific serologic type of enterococcus or diplostreptococcus was found associated with the lesions of nonspecific ulcerative colitis.

"Although one or more serologically related groups may be demonstrated by agglutination tests among enterococci isolated from intestines showing structural changes, members of such groups show differences in antigenic constitution as revealed by reciprocal agglutinin absorption inconsistencies.

"No correlation is apparent between fermentative activities, resistance to heat and other biologic characteristics of enterococci and serologic relationships.

"M. zymogenes is a variant of the enterococcus.

"Strains of enterococci serologically related to the type reported by Saunders as specific for gastric and duodenal ulcers were found in the intestine but more frequently in patients showing intestinal lesions than in normal adults."

TOOMEY, Cleveland.

IS A SPECIAL VARIETY OF STAPHYLOCOCCUS CONCERNED IN FOOD POISONING? JOSEPH STRITAR and EDWIN O. JORDAN. J. Infect. Dis. **56**:1 (Jan.-Feb.) 1935.

Stritar and Jordan demonstrate that there are no criteria for the differentiation of various types of staphylococci found in food poisoning.

TOOMEY, Cleveland.

EXPERIMENTAL RABIES IN WHITE MICE AND ATTEMPTED CHEMOTHERAPY: II. ANSON HOYT, ROY T. FISK, and CLINTON H. THIENES, J. Infect. Dis. **56**: 21 (Jan.-Feb.) 1935.

White mice were given rabies of a fixed type after intracerebral injection, but no drug could stop the spread of the virus.

TOOMEY, Cleveland.

THE PASSAGE OF BACTERIA FROM THE LUNGS INTO THE BLOOD STREAM. W. M. TUTTLE and PAUL R. CANNON, J. Infect. Dis. **56**:31 (Jan.-Feb.) 1935.

Bacterial suspensions of hemolytic streptococcus when introduced in the left lower lobe of the lung in fourteen healthy dogs quickly entered the blood stream directly, since the thoracic lymph remained sterile.

TOOMEY, Cleveland.

A SIMPLE METHOD OF ESTIMATING THE SEDIMENTATION RATE OF THE RED BLOOD CELLS. C. J. MCSWEENEY, Lancet **2**:756 (Oct. 6) 1934.

The blood obtained from a pinprick of the finger is taken up by means of an automatic pipet which already contains 3.8 per cent solution of sodium citrate. One volume of the solution to four volumes of blood are thoroughly mixed in the hollow of a glass slide, and the mixture is then allowed to run up into a calibrated capillary tube (6 inches [15.24 cm.] long and 1 mm. in bore) placed at an angle of 45 degrees. A column of blood 100 mm. in length is taken up, the upper end of the tube sealed with plasticine and the lower end stuck vertically into a lump of plasticine. After the blood has stood for an hour in a cool place the height of clear fluid is measured in millimeters, the reading obtained giving the sedimentation rate of the red cells.

LANGMANN, New York.

Nutrition

THE IODINE CONTENT OF POTATOES. JESSE F. MCCLENDON, EARL BARRETT and THOMAS CANNIFF, Biochem. J. **28**:1209, 1934.

The average iodine value of potatoes from the eastern section of Minnesota is 85 micrograms per kilogram and for the western section, 226 micrograms per

kilogram. The incidence of the simple goiter encountered among drafted men during the World War was 19 per thousand for the eastern section and 7.5 per thousand for the western section. This indicates an inverse relation between the iodine in potatoes and goiter in the drafted men. KUGELMASS, New York.

METABOLISM OF CAROTENE. BASHIR AHMAD, KHEM S. GREWAL and KHAZAN S. MALIK, Indian M. Gaz. **69**:320, 1934.

Carotene suspended in an aqueous solution of dextrose given to rats intravenously does not relieve the symptoms of vitamin A deficiency and does not cause the storage of detectable amounts of vitamin A in the liver. Similar experiments with dogs failed to show any transformation of injected carotene into vitamin A. The liver of the rabbit, however, seems to be able to make vitamin A from this source. KUGELMASS, New York.

THE SOYA IN EVERY HOSPITAL AND HOME. ROY H. MONIER, J. Missouri M. A. **31**:319 (Aug.) 1934.

This is an interesting discussion of the varieties of soy-bean suitable for human consumption and of the advantages of the soy-bean from the point of view of health, nutrition and economy.

After considerable difficulty a small quantity of two varieties (Easycook and Hahto) was obtained from the Department of Agriculture and planted on the grounds of five Missouri state institutions in 1929. In 1932, 1,600 bushels of these two varieties were produced. Their palatability was first tested on guests in the author's own home. During the past three years they have been served to the patients of five of the state institutions.

"Bread made with 20 per cent soy bean flour has proved very nutritious and palatable." Toasted, it is very popular. The flour is also used in cookies and cakes and in the making of chili. Recipes for baking, roasting and other methods of preparation are presented.

Besides the Easycook and Hahto varieties, the Mammoth, Midwest, Ito San and others are edible but require longer cooking.

The flour becomes rancid easily because of its high fat content. It is particularly valuable for its laxative effect and in the dietary of diabetic patients. The protein and fat content is higher than that found in any other food. The four essential amino-acids lycine, cystine, histidine and tryptophan are found abundantly present in the soy-bean. Soya milk is recommended for tuberculous children and persons suffering with gastric ulcer. BERGER, Kansas City, Mo.

CALCIUM CONTENT OF HUMAN MILK AFTER THE ADMINISTRATION OF CALCIUM, VIOSTEROL AND PARATHYROID EXTRACT. L. ROSSI, Clin. pediat. **16**:844 (Oct.) 1934.

The average calcium content of human milk is 22.82 micromilligrams per hundred cubic centimeters. There is no appreciable change in this value when calcium or viosterol is administered by mouth, but the calcium content increases by as much as 8.12 micromilligrams per hundred cubic centimeters when parathyroid extract is given. These conclusions are based on a study of five women. DOOLEY, New York.

VARIATIONS IN BLOOD CALCIUM AND PHOSPHORUS AFTER ADMINISTRATION OF STRONTIUM SALTS. P. VALENTINI, Clin. pediat. **16**:993 (Dec.) 1934.

The author reviews the physiologic properties of strontium salts and speculates on their possible therapeutic effect in the treatment of rickets. In his experiments rabbits showed significant increase in the amount of phosphorus and some increase in the calcium content of the serum after they had been given strontium chloride.

The simultaneous administration of viosterol by mouth or of parathyroid extract hypodermically did not change the results notably. The experiments reported are too few to warrant definite conclusions. DOOLEY, New York.

ASCORBIC ACID (VITAMIN C). MARCELLO BACHSTEZ, Gior. chim. ind. appl. **15**:510, 1933.

Bachstez has isolated a sizable quantity of cevitamic (hexuronic) acid or vitamin C from a species of Capsicum annuum (peppers from the Voghera region). The properties are identical with those indicated by the investigator who first isolated cevitamic acid from Hungarian paprika. KUGELMASS, New York.

RELATION BETWEEN THE BLOOD SUGAR AND THE SPINAL FLUID SUGAR IN THE NORMAL CHILD AND IN CHILDREN WITH VARIOUS DISEASES. L. W. PANAJOTTI, Riv. di clin. pediat. **32**:903 (Aug.) 1934.

The spinal fluid sugar in nine normal children averaged 46 mg. per hundred cubic centimeters (maximum, 56 mg.; minimum, 39 mg.). The spinal fluid sugar-blood sugar ratio averaged 0.58 (maximum, 0.75; minimum, 0.50). The findings in two cases of rickets and in four cases of bronchopneumonia were within the normal limits. In fourteen observations in cases of meningitis—tuberculous, meningococcic and pneumococcic—the spinal fluid sugar and the spinal fluid sugar-blood sugar ratio were low. In tuberculous children with marked malnutrition but no involvement of the nervous system the spinal fluid sugar and the spinal fluid sugar-blood sugar ratio were low. In cases of encephalitis, of chorea and of acute poliomyelitis the spinal fluid sugar and spinal fluid sugar-blood sugar ratio were often high. In other abnormalities of the central nervous system such as epilepsy, postdiphtheritic paralysis and cerebral tumor, the spinal fluid sugar varied in amount. HIGGINS, Boston.

AMMONIA AND UREA CONTENT AND THE p_H OF THE URINE OF HEALTHY INFANTS AND OF INFANTS WITH NUTRITIONAL DISTURBANCES. V. ANGELINI, Riv. di clin. pediat. **32**:1310 (Nov.) 1934.

In healthy infants the excretion of ammonia in the urine is constant, but the excretion of urea shows considerable variation, depending on the intake of protein.

For infants with digestive disorders, especially acute alimentary intoxication, the amount of ammonia excreted tends to increase and the amount of urea to decrease. With improvement of the symptoms the amount of ammonia excreted tends to approach the normal value for healthy infants. HIGGINS, Boston.

DISTRIBUTION OF CALCIUM AND PHOSPHORUS IN DIFFERENT ORGANS AND TISSUES OF RATS IN DEFICIENCY AND EXCESS OF PARATHYROID HORMONE. PIETRO MOLINARI-TOSATTI, Sperimentale, Arch. di biol. **88**:504, 1934.

The calcium content in thyroparathyroidectomized rats is slightly diminished in the bones and liver, definitely diminished in the brain, heart, lungs, muscles, kidneys and skin and slightly increased in the spleen. The phosphorus content is slightly increased in the bones, brain, lungs and kidneys and definitely increased in the skin; it is definitely diminished in the heart and less so in the liver, spleen and muscles. Treatment with parathormone causes a decrease of calcium in the liver, an increase in the spleen and kidneys and no change in the heart, lungs and skin. The phosphorus decreases in the bones and more in the heart and spleen; it is almost unchanged in the liver, muscles and skin and slightly increased in the brain, lungs and kidneys. KUGELMASS, New York.

ACID-BASE EQUILIBRIUM IN DYSTROPHIC INFANTS. CARLOS SALAZAR DE SOUSA, Arch. de pediat., Rio de Janeiro **6**:845 (June) 1934.

In twelve infants from 1 to 4 months of age the p_H was 7.396 and the alkali reserve was 54.6 per cent. In the same number of children from 7 to 12 months of age the p_H was 7.389, and the alkali reserve was 47.7 per cent.

SANFORD, Chicago.

COW'S MILK AND ITS DERIVATIVES IN THE FEEDING OF THE INFANT. R. ORTEGA A., Rev. chilena de pediat. **5**:617 (Nov.) 1934.

Fresh cow's milk as consumed in Santiago, Cuba, is generally of such inferior quality that its employment in infant feeding is inadvisable. Only hospitals and welfare stations at present receive properly safeguarded milk. Suitable milk is produced in establishments under municipal control.

If fresh pure cow's milk is not obtainable, dried milk should be used. The manufacturers have abandoned the practice of furnishing the laity with feeding directions with their product.

Legislation for the sanitary control of milk is advisable.

SCHLUTZ, Chicago.

CONDITION OF THE ENDOCRINE GLANDS OF RATS DURING AVITAMINOSIS A. M. S. MITZKEWITCH, Arch. f. exper. Path. u. Pharmakol. **174**:339, 1934.

In rats with avitaminosis A the pituitary gland was hypertrophied but appeared histologically normal. The thyroid gland was hypertrophied but appeared to be in a state of hypofunction. The testes were decreased in size; ripe spermatozoa were rare, and the generative epithelium of the seminal canals was hypertrophied. Females were sterile, but the estrual cycles proceeded normally. The ovaries were normal but small. The adrenals of the males were hypertrophied.

KUGELMASS, New York.

ARE THE ACID WHOLE MILKS TO BE RECOMMENDED FOR COMMON USE IN THE NUTRITION OF NORMAL INFANTS? ERICH MÜLLER, Arch. f. Kinderh. **102**:129 (June 22) 1934.

In the past few years the use of acidified whole milk in infant feeding has been increasing rapidly. To the acid whole milk some form of sugar is added, and sometimes cereal is also added. Müller wrote to the leading pediatricians of Germany asking them whether they recommended the adoption of acidified whole milk as the standard feeding for normal infants. This article contains answers from the following: G. Bessau, H. Beumer, H. Brüning, R. Degkwitz, J. von Duzár, G. Fanconi, E. Hainiss, Franz Hamburger, H. Kleinschmidt, E. Moro, E. Rominger, A. Reuss, K. Stolte and H. Vogt. As might be expected, the opinions varied widely. Some of the pediatricians answered strongly in the affirmative and others just as strongly in the negative. Others modified their answers. Many of them stated that they had used acidified whole milk for some time, with excellent results, but hesitated to recommend any one type of feeding as universal, because each infant should be fed as an individual. LEMASTER, Evanston, Ill.

ARREST OF SEVERE HEMORRHAGES IN ALL FORMS OF HEMORRHAGIC DIATHESIS AND IN HEMOPHILIA BY PARENTERAL ADMINISTRATION OF VITAMIN C. A. BÖGER and H. SCHRÖDER, München. med. Wchnschr. **81**:1335 (Aug. 24) 1934.

The authors previously reported the beneficial therapeutic effect of the parenteral administration of vitamin C on capillary bleeding. They now report the effect of cevitamic acid in other hemorrhagic diatheses. In a case of Schönlein-Henoch's purpura the daily intravenous administration of 100 mg. of ascorbic acid caused a rapid disappearance of the symptoms of the capillary toxicosis. The oral admin-

istration of vitamin C in this case had been ineffective. Vitamin C may be destroyed by the bacteria in the duodenum, or its absorption may be diminished by inflammation of the intestinal mucosa or the decreased intestinal motility which frequently occur in the avitaminosis.

In a case of hemophilia intestinal hemorrhages were stopped by the daily intravenous administration of 150 mg. of cevitamic acid. No ill effects resulted from the larger doses. In a patient, aged 60 years, with essential thrombocytopenia (no platelets could be found in three separate counts) daily intravenous doses of ascorbic acid stopped the widespread severe hemorrhages in four days. After the hemorrhages were stopped, the blood platelets gradually increased. From this case the authors conclude that the permeability of the capillaries, in addition to the decrease in platelets, is of importance in Werlhof's thrombocytopenia. In another patient with hemophilia severe hemorrhages were controlled with ascorbic acid.

BRAHDY, Mount Vernon, N. Y.

ENTERITIS AND THE APPLE DIET. M. SUSSMANN, München. med. Wchnschr. **81**:1857 (Nov. 29) 1934.

The author used the apple diet recommended by Heisler and Moro for the treatment of enteritis with excellent results. Although other authors have used baked apples and bananas, Sussmann limited himself to grated ripe apples or to a prepared apple powder. A large apple was grated for the patient every two hours, and dark tea with saccharin was offered if the patient was thirsty. After one or two days the diarrhea was under control. Toast, soups and lean meat were added to the diet, and the amount of apple was decreased.

BRAHDY, Mount Vernon, N. Y.

METABOLIC OXIDATION AND RADIATION. MAURICE COPISAROW, Protoplasma **21**:73, 1934.

Ultraviolet radiation is a general feature of the normal metabolism of organized matter. Radiation is associated with the chemical function of respiratory enzymes (oxidase and dehydrogenase). Products of metabolism radiate by virtue only of the active enzymes accompanying them. No radiation is observed under conditions which temporarily or permanently inactivate the enzymes. Cholesterol, vitamins and hormones as such are devoid of radiation. Thirty-nine references to the literature are included.

KUGELMASS, New York.

THE PHYSIOLOGY OF GASTRIC SECRETION: CHANGES IN RELATION TO THE TIME FACTOR IN FEEDING. B. I. BAYANDUROV, Ark. biol. nauk. **34**:125, 1934.

Strictly regulated conditions of quantity, quality and periodicity of feeding of dogs with Pavlov pouches produced a remarkable stability in the rate, volume and composition of the gastric secretion. Deviations from the accustomed (conditioned) system of feeding produced changes in the secretion in regard to the latent period of stimulation, the relative length of the period of active secretion and the maximum acidity and enzyme content.

KUGELMASS, New York.

RELATIONSHIP BETWEEN DISEASES OF THE PANCREAS AND THE HYDROLYSIS OF CARBOHYDRATES IN THE FECES. KUNIO SEKIKAWA, Tohoku J. Exper. Med. **24**:72 (Sept. 28) 1934.

The carbohydrate in human feces hydrolyzable by dilute acid is normally 50 mg. per gram of dried feces; in dogs, it is from 80 to 190 mg. After ligation and section of the pancreatic duct in dogs it is increased to from 190 to 230 mg., and after the establishment of an external pancreatic fistula it increases to from 240 to 500 mg., with the appearance of granules of starch in the feces. The microscopic demonstration of granules of starch in the feces of human beings on a

normal diet is evidence of functional or organic disease of the pancreas. Numerous reports of cases indicate that an increase in the hydrolyzable carbohydrate of the feces in human beings, accompanied by other clinical evidence referable to the pancreas, is strong evidence for the existence of a chronic pancreatic disease.

KUGELMASS, New York.

AN EXPERIMENTAL STUDY OF CERTAIN PREPARATIONS OF ORANGE (AND OF LEMON) FROM THE POINT OF VIEW OF THE ANTISCORBUTIC EFFECT. ROLF BERGMAN, Acta pædiat. **15**:285 (June 5) 1934.

Although the average Swedish diet contains enough garden vegetables to prevent frank scurvy, the development of the concept of "latent scurvy" has called attention to the need of a higher concentration of vitamin C than that found in cabbage, spinach, lettuce, radishes and the like. In the Scandinavian peninsula citrus fruits are apt to be expensive and are frequently hard to procure. Hence repeated efforts have been made to prepare a concentrate of vitamin C which would be physiologically potent and economically feasible. These attempts have been generally unsuccessful because of the extreme instability of the antiscorbutic principle. Vitamin C is rendered inert by exposure to air, by heat and by alkali, as well as by the natural fermentation which occurs in the citrus fruits in which it is found. Chemicals which inhibit fermentation also destroy the vitamin. A few scientifically satisfactory methods of conserving the antiscorbutic potency of foods have been devised; most of these present obstacles which render them unsuitable for commercial application.

There has appeared recently on the Swedish market a Spanish concentrate of orange juice labeled Naranjina. The details of its preparation are obscure. Bergman made carefully controlled biologic tests of the antiscorbutic potency of this product, using several groups of guinea-pigs. All the animals depending on Naranjina for protection died of scurvy.

MCCUNE, New York.

MINIMUM DOSE OF VITAMIN D REQUIRED TO CURE AND TO PREVENT RICKETS. J. J. SOER, Acta pædiat. **15**:307 (June 5) 1934.

In the studies reported in this paper the author employed what he regarded to be physically verified vitamin D. This was "substance L" prepared by Reerink and Van Wyk through the action of radiant energy of long wavelength (from 2,800 to 3,100 angstroms) on ergosterol. This material has an antirachitic potency of 23,000 international units per milligram. It is closely related to a preparation evolved by Bourdillon and Webster which contains 40,000 international units per milligram, and also to a similar substance produced for the first time by Windaus.

The average daily dose of L substance required to cure rickets in children was 0.05 mg. This was equivalent to 0.001 mg. per kilogram of body weight daily. The occurrence of healing was determined by increase in the concentration of serum phosphorus and by the appearance of the wrists in roentgenograms taken at weekly intervals. The potency of L substance was not diminished when it was incorporated into tablets in which cocoa butter was employed as a vehicle and to which chocolate was added for palatability. The average daily dose of L substance required to prevent rickets in infants was 0.02 mg. This is equivalent to 800 international units.

MCCUNE, New York.

COMPARATIVE ANTIRACHITIC EFFICIENCY OF IRRADIATED ERGOSTEROL AND COD LIVER OIL FOR THE CHICKEN AND A DESCRIPTION OF A MORE RELIABLE METHOD FOR THE DETERMINATION OF RACHITIC WEAKNESS OF THE LEGS OF BABY CHICKENS. M. J. L. DOLS, Arch. néerl. de physiol. **19**:290, 1934.

Viosterol dissolved in peanut oil is less effective in protecting chickens against rachitic weakness of the legs than the equivalent amount in rat units of cod liver oil. This finding confirms those of other investigators.

KUGELMASS, New York.

VITAMIN A IN BLOOD SERUM AND IN MOTHER'S MILK. J. G. MENKEN, Maandschr. v. kindergeneesk. **4**:22 (Oct.) 1934.

In this article, the summary of a comprehensive thesis, the author points to the importance of vitamin A for health and growth of the child; diseases caused by deficiency of vitamin A are frequent in the Dutch colonies but not in The Netherlands. The author describes the chemicocolorimetric method for the determination of vitamin A and carotene in blood serum and milk; i. e., by the addition of ten times the volume of 96 per cent alcohol and extraction of the alcohol with petroleum and ether. In human blood serum and milk vitamin A is generally and carotene is always present. For well fed persons a higher value for vitamin A and carotene is shown than for more poorly situated persons. A relation though not an absolute one exists between the vitamin A and the carotene content of the blood serum and milk. No definite relation between these contents and certain diseases, with perhaps the exception of eczema, could be demonstrated. Pregnant and nursing women and children should be given vitamin A, especially in the winter; colostrum contains much vitamin A and carotene, and so it is of great value for the nutrition of the baby. A large part of the population receives an insufficient amount of carotene and vitamin A.

VAN CREVELD, Amsterdam, The Netherlands.

Prenatal Conditions

FAMILIAL CLEIDO-CRANIO DYSOSTOSIS. JULIANNA R. TATUM, Am. J. M. Sc. **188**:365 (Sept.) 1934.

Defective clavicles were described as early as 1765, but the condition was called cleidocranial dysostosis in 1897. A case of cleidocranial dysostosis is reported, with the results of roentgen and blood chemistry studies. A family tree and brief notes on members of the immediate family are given. The blood phosphorus and blood calcium of these seven persons are compared with the values in similar cases described by other writers (eleven subjects).

HENSKE, Omaha.

CONGENITAL DIAPHRAGMATIC HERNIA; CASE REPORT. J. FRIEDMAN, Am. J. Roentgenol. **33**:36 (Jan.) 1935.

Friedman gives a detailed report of a baby weighing 6 pounds and 6 ounces (2,891.64 Gm.) at birth. The baby appeared normal until 9 days of age, then showed rapid breathing, became cyanosed and died on the tenth day. Roentgen examination showed a honeycomb network occupying the entire left side of the chest. Postmortem roentgen examinations and autopsy showed the stomach, intestines, pancreas and spleen in the left pleural cavity; the heart and mediastinal structures deviated to the right side of the chest. The herniation was permitted by a congenital defect in the left side of the diaphragm, measuring 4 cm. in diameter.

AGENESIA OF THE ABDOMINAL MUSCLES. S. J. MCCLENDON, Arch. Pediat. **51**:673 (Oct.) 1934.

A case of agenesia of the abdominal muscles is reported because of the rarity of the condition and because of the association of anomaly of the genito-urinary tract which often accompanies absence of the abdominal muscles.

WADDELL JR., University, Va.

CONGENITAL PULMONARY CYSTS ASSOCIATED WITH CONGENITAL HEART DISEASE AND HYDRONEPHROSIS. LEON SOLIS-COHEN and SAMUEL LEVINE, Arch. Pediat. **51**:758 (Dec.) 1934.

Two cases of congenital pulmonary cyst are reported. In one case the cyst was an example of the type that causes marked symptoms in early infancy. This

condition was found to be associated with concomitant tetralogy of Fallot and hydronephrosis, closely related to a syphilitic background.

The second case was discovered accidentally in adult life, and the condition of itself caused no marked symptoms. The authors discuss the pathogenesis, the theory of causation and the differential diagnosis.

WADDELL JR., University, Va.

CONGENITAL COXA VARA. ISADORE ZADEK, Arch. Surg. **30**:62 (Jan.) 1935.

A complete review of the history of congenital coxa vara is presented. The various theories dealing with the etiology of this condition are presented. The complete study of the ten cases reported stresses the importance of the history and the roentgen appearance. The proper treatment consists of two surgical phases: (1) Bony union should be produced in the defective portion of the neck of the femur by drilling, and (2) when this union is secure, the depressed neck of the femur should be elevated by a subtrochanteric wedge osteotomy.

KAISER, Rochester, N. Y.

PREMATURE INFANTS; A REPORT OF 1,623 CONSECUTIVE CASES. JULIUS H. HESS, Illinois M. J. **67**:14 (Jan.) 1935.

From 1922 to Dec. 31, 1933, 1,623 infants were admitted to the Premature Infant Station at the Sarah Morris Hospital for Children, Chicago. A study of these cases showed that special care must be taken of premature infants as early as the time of delivery. Extreme caution should be exercised to prevent infection, to avoid an initial lowering of body temperature and to guard against asphyxia. The infant should be placed in a heated bed and all ordinary procedures performed without removing it. Feeding is carried on by means of a bottle with a small nipple, a medicine dropper or a catheter until the infant is strong enough to nurse at the breast. Food is withheld the first twelve hours of life. During the second twelve hours four feedings of from 2 to 10 cc. of water and two feedings of from 2 to 10 cc. of milk are given. From the second to the twentieth day eight or more feedings are given in twenty-four hours, using a total of from 20 to 40 cc. of milk per kilogram of body weight. The amount is gradually increased as tolerated by the infant. Human milk is essential. Carbohydrates are added in amounts of 2 per cent, gradually increasing to 5 per cent. The administration of orange juice and cod liver oil and exposure to the ultraviolet rays are started during the third week and either egg-yolk or iron during the fourth week. Water is given in amounts varying up to a total of one sixth the body weight in twenty-four hours.

Hypodermoclysis, oxygen therapy, blood for intramuscular injection and cardiac stimulants must be available when indications for their use arise.

Syphilis was present in 8.2 per cent of the infants. Of 1,134 infants dismissed from the hospital 128 were considered to have had intracranial hemorrhage, and it was present in 128 of the 386 infants on whom autopsy was performed.

POTTER, Chicago.

REDUCTION OF PREMATURE INFANT MORTALITY. STEWART H. CLIFFORD, J. Pediat. **5**:139 (Aug.) 1934.

Following the work of Scammon and Calkins, Clifford measured the occipitofrontal diameter of the fetal head roentgenologically in six hundred cases and found that by this method the age and weight of the fetus in utero could be approximately determined. This information is of great value in deciding on the optimum time for the induction of labor, since it is definitely established that the mortality of premature infants is inversely proportional to the weight of the infant at birth. The influence of various obstetric factors on the mortality of 958 premature infants was also studied. Complications of pregnancy in the mother apparently affected the fetal viability only if the placental circulation was influenced.

The mortality of premature infants was much lower in those delivered by vertex presentation and low forceps than in those delivered by cesarean section or breech extraction. The administration of morphine to the mother within four hours before delivery also greatly increased the mortality. The practical application of these findings gave excellent results in the author's experience during 1933.

LEMASTER, Evanston, Ill.

THE PULMONARY LESIONS ASSOCIATED WITH INTRAUTERINE ASPHYXIA. MAURICE ROSENTHAL, J. Pediat. **6**:71 (Jan.) 1935.

In one hundred consecutive autopsies on stillborn and new-born infants, anatomic lesions of intra-uterine asphyxia were found in eighty. The pulmonary lesions consisted of aspiration of the contents of the amniotic sac (11 per cent), desquamation of bronchial epithelium (31 per cent) and congenital pneumonia (6 per cent). Of sixty-two new-born infants who died within the first two weeks of life, fifty showed clinical evidence of asphyxia, and twenty-three showed pulmonary lesions sufficient to account for the asphyxia.

LEMASTER, Evanston, Ill.

INCONTINENCE OF URINE DUE TO URETERAL ECTOPIA. AUGUSTUS RILEY and EUGENE A. GASTON, New England J. Med. **211**:666 (Oct. 11) 1934.

A 16 year old schoolgirl complained of constant dribbling of urine, both nocturnal and diurnal, since infancy. Associated with this she passed normal amounts of urine from the bladder from four to six times a day and had the usual feeling when the bladder was full, with complete relief of this after voiding. Examination showed a "tiny opening" just to the right of the external urinary meatus, through which urine dribbled at periodic intervals, especially on standing or straining. Cystoscopy revealed what was believed to be the internal opening of an accessory urethra, midway between the internal urethral orifice and the right ureteral opening. Otherwise the bladder appeared perfectly normal, with two normal ureteral orifices normally placed. Five attempts were made to stop the dribbling by the injection of caustics. The patient was operated on. As long as the retention catheter remained in the bladder there was no urinary dribbling. However, on removal of the catheter the dribbling continued to be as bad as before operation.

The bladder was filled with a 2 per cent solution of mercurochrome, and it was noted that the escaping urine was not colored. The patient was given two ampules of diodrast intravenously. Roentgenograms taken at periodic intervals revealed on the right side above the normal pelvis of the kidney a small, poorly filled but definite third renal pelvis. Unfortunately, only a very slight and unsatisfactory visualization of the attached ureter was possible.

After three unsuccessful attempts, the para-urethral sinus was catheterized. The complete filling of both ureters and pelves with a 12.5 per cent solution of sodium iodide revealed that the ectopic ureter led into a distinct renal pelvis, infantile in type, not communicating with the normal renal pelvis which was immediately below.

Following operation the patient made an uneventful recovery save for slight sepsis due to the wound which was easily controlled. Since operation she has been completely free from all signs of urinary dribbling.

An excellent review of the literature and a thorough discussion of the condition follow.

GENGENBACH, Denver.

COARCTATION OF THE AORTA IN FATHER AND SON. WILLIAM G. WALKER, New England J. Med. **211**:1192 (Dec. 27) 1934.

The father was first seen at the age of 39. He complained of feeling "all in." This feeling came on five years before. For one year he had experienced dyspnea on exertion and palpitation and pain around the heart following exercise. The

pulse rate was 80. The blood pressure (right arm) was 186 systolic and 108 diastolic. The cardiac rhythm was regular. A systolic murmur was heard over each valvular area, being loudest at the second interspace on the right. This murmur was transmitted to the right side of the neck. Tests of the urine and blood, including the Wassermann test, gave essentially negative results.

Following an absence of three years, the murmur was still transmitted to the right side of the neck. No pulsation could be felt over the abdominal aorta. The blood pressure in the right arm was 158 systolic and 82 diastolic, and the blood pressure in the left femur was 108 systolic and 94 diastolic.

At fluoroscopic examination of the chest the ascending and transverse aorta pulsated vigorously. Just below the aortic knob no pulsation was seen. An x-ray film of the chest revealed the typical scalloping of the ribs posteriorly.

The son when first seen at the age of 15 complained of being "all run down." Dizziness was noticed at times on suddenly arising in the morning. Dyspnea was induced by a little sustained effort, and palpitation developed if he ran. The Wassermann and Kahn reactions of the blood were negative. Over the chest anteriorly, pulsations were visible at the first interspace on the left and the second interspace on the right, and there were vigorous pulsations of the epigastrium. Below the scapulae and over the lower part of the right axilla, pulsating vessels could be felt. The blood pressure in the right arm was 166 systolic and 108 diastolic. The blood pressure in the left femur was 130 systolic and 116 diastolic.

Fluoroscopy of the chest later showed forcible pulsations of the ascending and the transverse aorta. In the region of the isthmus there was a constriction, and no pulsation was visible. As would be expected from the shorter duration of the process in this patient, in the roentgenogram of the chest the scalloping of the ribs is not so deep.

The mother, the maternal grandmother and a maternal aunt of the son have hypertension of the usual type.

GENGENBACH, Denver.

THE PROBLEM OF THE PREMATURE INFANT. RALPH M. TYSON, New York State J. Med. **34**:811 (Sept. 15) 1934.

A study of four hundred and sixty-nine premature infants is reported. The causes of prematurity, the influence of the gravida, the effects of delivery, the importance of the weight at birth and the causes of death are considered. Digestive disturbances are a serious problem in new-born infants and can often be prevented by careful attention to feeding in the first ten days. Even minor digestive disturbances should receive immediate attention. Weekly blood counts disclose a more rapid fall in hemoglobin and red cells than occurs in full-term infants. Breast milk is still the food of choice. Close attention should be given to temperature and humidity.

AIKMAN, Rochester, N. Y.

COARCTATION OF THE AORTA. JOHN F. BEATTY, Northwest Med. **33**:332 (Sept.) 1934.

The patient was a man, aged 22, who had always been active in athletics. Without warning symptoms he felt a sensation as of a foreign body in the throat. This was soon followed by convulsions and left-sided hemiplegia. There was an absence of the pulse in the abdominal aorta, with an excessive pulsation in the vessels of the neck. The blood pressure in the right arm was 160 systolic and 90 diastolic. There was a thrill over the base of the heart. The blood pressure was not readable in the lower extremities. The patient died. Autopsy showed a complete obstruction at the ductal aortic junction. A photograph is included.

SCOTT, Philadelphia.

CONGENITAL VALVULAR OBSTRUCTION IN THE PROSTATIC URETHRA. R. RUTHERFORD and JOHN H. FOLLOWS, Brit. J. Child. Dis. **31**:297 (Oct.-Dec.) 1934.

An instance of this condition is described in a boy who was observed intermittently from the age of 12 weeks until he died at about 11 months of age.

Autopsy revealed bilateral hydronephrosis, very little renal tissue remaining. Both ureters were distended to the size of the small intestine, and the bladder was extremely hypertrophied. Two valvelike membranes were found stretched across the junction of the prostatic and the membranous portion of the urethra.

LANGMANN, New York.

STUDIES ON PRENATAL LESIONS OF STRIATED MUSCLE AS A CAUSE OF CONGENITAL DEFORMITY. D. STEWART MIDDLETON, Edinburgh M. J. **41**:401 (July) 1934.

Middleton confines his study to the following deformities: congenital tibial kyphosis, congenital high shoulder and myodystrophia foetalis deformans.

Three young children from infancy to 3½ years of age furnished the instances of congenital tibial angulation. The clinical description of the deformities is given and discussed, and the pathologic tissue changes are described. This deformity is said to be the result of failure of the later developmental stages of the muscles of the calf during intra-uterine life.

Two young children with congenital elevation of the scapula (Sprengel's shoulder) furnish the illustrations for the author's study of the second group. The microscopic changes in the muscles of the shoulder girdle seem to represent an interruption of the normal differentiation of the muscle fibers at the myoblastic stage. The anomaly not only is muscular but involves all the cervical mesodermic structures.

Multiple congenital contractures of joints make up the conditions of the third group, seen in seven young children. The deformities included clubhands, clubfeet, contractures of knees and hips, dislocation of the hip and scoliosis. The cause of the deformities is fatty degeneration of the muscles of the extremities during intra-uterine life. The author applies the term "myodystrophia foetalis deformans" to these multiple deformities and thinks that they are analogous to the muscular dystrophies of later life.

NEFF, Kansas City, Mo.

CONGENITAL OBSTRUCTION OF THE ESOPHAGUS. HAZEL H. CHODAK GREGORY and G. T. CALTHROP, Proc. Roy. Soc. Med. **28**:141 (Dec.) 1934.

This condition is reported in a child 12 months old. He had been kept four months at a fever hospital after recovery from measles in order to try various foods, after which he was transferred to a children's hospital as a patient with obstinate marasmus. Fluid was generally swallowed and retained, but solid food was invariably regurgitated in great quantities. Saliva was regurgitated. A roentgenogram showed that a teaspoonful of a barium sulphate meal stopped at the seventh rib posteriorly. Above this point the esophagus was dilated. When more meal was swallowed a narrow constriction ¼ inch (0.64 cm.) in length filled up. Distal to the constriction the esophagus was of normal width. A description of the treatment and pictures taken after the barium sulphate meal accompany the report.

WILLIAMSON, New Orleans.

CONGENITAL ELEVATION OF THE DIAPHRAGM. A. G. MAITLAND-JONES, Proc. Roy. Soc. Med. **28**:143 (Dec.) 1934.

A girl, aged 5 years, was taken to the hospital on account of a chronic cough which she had had for some months. At the left base the percussion note was impaired, and the breath sounds were diminished. A roentgenogram showed that the left half of the diaphragm was raised considerably and moved only slightly with respiration. There was no paradoxical movement. Following the ingestion of a bismuth meal the stomach was seen to lie just below the left cupola of the diaphragm. Cervical ribs and, on the right side, an azygos pulmonary lobe were also present.

WILLIAMSON, New Orleans.

Diseases of the New-Born

PROBLEMS OF THE NEW-BORN. BARNET E. BONAR, J. Pediat. **5**:216 (Aug.) 1934.

The recent literature on the antenatal and postnatal problems of the mother and child is critically reviewed. It is shown that as yet no substantial decrease in the number of maternal or neonatal deaths has been achieved. Closer cooperation between lay organizations and physicians is needed. Recent advances in knowledge concerning the following medical aspects of antenatal care are discussed: nutrition, anemia, thyroid disturbances, diabetes, infections, heart disease and the toxemias. The author considers the antenatal problem primarily medical and believes that it can be solved satisfactorily only under sane and conservative medical direction.

LEMASTER, Evanston, Ill.

CONGENITAL ICHTHYOSIS. G. RICHARDS WILLIAMSON, J. Pediat. **5**:484 (Oct.) 1934.

A case of congenital ichthyosis is reported. A photomicrograph of a section of the skin taken for biopsy is reproduced. The literature on this subject is briefly reviewed.

LEMASTER, Evanston, Ill.

PHYSIOLOGIC ICTERUS OF THE NEW-BORN AND ITS PREVENTION BY THE METHOD OF KEIFER. P. RETTAGLIATA, Prat. pediat. **12**:485 (Nov.) 1934.

After a review of the literature relating to physiologic icterus of the new-born and the possible function of vernix caseosa, the author describes an experiment in which he subjected 50 babies to the usual postnatal bathing while he clothed a comparable group of 50 babies without bathing them. In nearly two thirds of the babies who were bathed jaundice developed, while it occurred in less than one third of the infants who were not bathed. Also the jaundice was less severe in the babies who were not bathed. From this he concludes that the bathing of new-born infants may be an unphysiologic procedure.

He also studied the occurrence of icterus in an unselected group of 1,000 babies and found that it appeared in 100 per cent of the infants whose weight at birth was less than 2,500 Gm.; in 9.45 per cent of those whose weight at birth was between 2,500 and 3,000 Gm., and in only a little more than 3 per cent of those who weighed more than 3,000 Gm. at birth. Statistically, the greater the physiologic loss of weight after birth the greater the tendency to jaundice. Jaundice occurred twice as often in boys as in girls in this group.

DOOLEY, New York.

BLOOD CALCIUM IN THE NEW-BORN. N. PALACIOS COSTA, FLORENCIO ESCARDÓ and SAMUEL SCHERE. Rev. Soc. argent. de biol. **10**:273 (Sept.-Oct.) 1934.

The authors made daily determinations of the calcium content of the blood in new-born infants. They found in general that the calcium content of the blood increased gradually each day during the first week of life. The average increase was about 1 mg. during the week. There were many variations, and in some cases the values were lower on subsequent days; in all the cases, however, after a week the calcium content of the blood was higher than on the first day. In premature babies the smaller the baby the lower the calcium content of the blood, and it increased with the weight. The relation of the calcium content of the blood of the mother to that of the infant determined in thirty cases revealed that the calcium content of the mother's blood was higher in all but three cases, the variations ranging from 0.1 to 2.5 mg. with an average of 0.5 mg.

HERRON, Spokane, Wash.

Spontaneous Pneumothorax in the New-Born. Josef Riedweg, Monatschr. f. Kinderh. **61**:1, 1934.

The writer reports twelve cases in which pneumothorax occurred spontaneously in new-born infants and includes two roentgenograms. In the majority of these cases labor was difficult. In contrast to the usual clinical picture of pneumothorax, which is grave and alarming, these infants seemed only mildly affected. In fact, in most instances the diagnosis would never have been made had it not been for the roentgenogram taken as a routine. Pneumothorax should be suspected if immediately after birth cyanosis and dyspnea become evident. But the condition may be present with no symptoms. In all the twelve cases the air was quickly absorbed.

Gerstley, Chicago.

Case of Hematoma of the Umbilical Cord. K. Marang, Nederl. tijdschr. v. geneesk. **78**:3952 (Sept. 1) 1934.

A case is recorded of hematoma of the umbilical cord associated with early rupture of the membranes (a week before birth) and asphyxia of the child.

van Creveld, Amsterdam, The Netherlands.

Acute Infections

Bronchiectasis as a Source of Scarlet Fever Dissemination. Harvey Spencer, New England J. Med. **212**:196 (Jan. 31) 1935.

Following scarlet fever, persistent discharge from infections of the nose, middle ear, mastoids, cervical glands and other draining lesions may be the source from which scarlet fever is spread by contact to nonimmune persons.

Spencer reports a case of scarlet fever in which the source of the contagion was apparently a child who had suffered from bronchiectasis for two years and who when seven weeks convalescent from scarlet fever harbored Streptococcus haemolyticus in the pus from his lung. The patient who contracted the disease was in intimate contact with the child.

The nurse-maid caring for the two children contracted atypical scarlet fever of short duration. An attempt to confirm bacteriologically the source of infection failed.

Gengenbach, Denver.

Prophylaxis of Malaria in Childhood. Barrowman, Bull. Assoc. internat. de pediat. prevent. **4**:41, 1934.

It is difficult to determine the toll which malaria exacts among children of the tropical East; the disease may complicate so many other conditions that its influence on vital statistics cannot be accurately appraised, but clinicians recognize that it is among the young that uncomplicated malaria more often reaches a fatal issue. Among the great masses of the native races only a small percentage of these deaths come to the attention of a medical practitioner, and in still fewer cases is the blood examined.

Watson has shown that a reduction in the number of cases of malaria is accompanied by a remarkable decline in the death rate registered for other diseases of childhood. Another effect of malaria on child life must be considered: Where the disease is endemic, women conceive rarely and few carry to full term. In certain areas in India, Christopher has found 100 per cent of children under 2 years of age infested with parasites.

Congenital infections are extremely rare, even in hyperendemic regions. The results of thirty years of antimalaria work are reflected in the decline of the mortality rate from 300 to 18 among adults and from 900 to 130 for children. Barrowman classifies control under three heads: permanent measures, temporary expedients and the administration of drugs.

Amesse, Denver.

NASAL ANTIDIPHTHERIA VACCINATION. ANTONIO SABELLI, Rev. Soc. argent. de biol. **10**:378 (Nov.) 1934.

Sabelli presents an intranasal method of antidiphtheritic vaccination, which is of value for persons with asthma particularly. The intervals between doses and the increase in dosage are the same as when immunization is produced by subcutaneous injection. Four applications at from fifteen to twenty-one day intervals are all that are necessary; this produced negative Schick reactions in 95 per cent of the author's cases. His evidence is not sufficiently inclusive.

HERRON, Spokane, Wash.

FURTHER OBSERVATIONS ON PROPHYLACTIC VACCINATION AGAINST PERTUSSIS. W. KAUPE, Med. Klin. **31**:79 (Jan. 18) 1935.

In an infants' home in Bonn, two girls aged 2 years introduced pertussis and caused the infection of four babies aged 7, 3, 3 and 2 months old, respectively. These four babies were treated by vaccination early in the course of the disease and recovered after very mild illnesses. Twelve other babies, who were in close contact with the infected ones, were given prophylactic vaccinations and escaped the disease entirely. Seven of these twelve were less than 1 year old, and one was only 1 month old.

DOOLEY, New York.

ANIMALS AS CARRIERS OF PARATYPHOID BACILLI: SIGNIFICANCE FOR HUMAN BEINGS. H. DAVID, Wien. klin. Wchnschr. **47**:1377 (Nov. 16) 1934.

David points out that there are different types of paratyphoid bacilli with distinct morphologic, biochemical, serologic and pathogenic characteristics and that the type determines to a large extent the symptoms of the disorder. Thus paratyphoid, the symptoms of which resemble typhoid, is generally caused by types A and B Schottmüller, whereas Breslau, Gärtner, Newport or similar strains of bacilli are usually detected in the gastro-intestinal forms. In animals, paratyphoid is caused either by types the pathogenicity of which for human subjects has not been proved as yet or by strains that cause the acute form in human subjects and are designated as the enteritis types (Breslau, Gärtner, Newport and others). After calling attention to the fact that these bacilli may not only cause disorders in the intestines of animals but also invade the internal organs and the muscles, the author points out that the ingestion of meat from animals that have had an enteritis infection may cause meat poisoning in human subjects. Animals may become carriers of enteritis bacilli without showing symptoms of disease, and foods may become contaminated with their excretions, or their meat may not be recognized as a possible source of disease. Moreover, cows that are carriers may produce contaminated milk, and milk products may likewise become infected. The author calls attention to the increasing incidence of food poisoning caused by meat from infected poultry and by eggs. Reports about eggs as sources of infections with Gärtner and Breslau bacilli have come from England, France and, particularly, Germany. Infections with Breslau and Gärtner bacilli have been traced also to rats and mice as carriers. In discussing the measures for the prevention of paratyphoid-enteritis infections the author stresses the necessity of eliminating animal carriers, and he recommends periodic examinations of live stock in order to detect them.

ABT, Chicago.

METABOLISM OF WATER IN DIPHTHERIA (THE REACTION OF MCCLURE AND ALDRICH). R. S. CHERMAN, Sovet. pediat., no. 1, 1934, p. 78.

Cherman examined 110 patients and made 390 tests. The time of resorption of the papule in the first days of the disease is from forty to fifty minutes; at the end of the disease and during convalescence the time of resorption is from seventy to ninety minutes. Accidents with serum shorten the time of resorption to from twenty to forty minutes.

SEMENENKO-MCKHANN, Boston.

DYSENTERY IN DENMARK. KNUD BOJLÉN, Comm. Inst. serothérap. de l'État Danois, Copenhagen **24**:1, 1934.

The work deals with the bacteriology and epidemiology of the Sonne and Flexner bacilli which were responsible for all but 3 cases of dysentery in Denmark during the years 1926 to 1933. Three cases which were due to the Shiga-Kruse bacilli were imported from outside Denmark. The Sonne dysentery bacilli were isolated from 751 patients and the Flexner bacilli from 247 patients. The bacilli were isolated partly in sporadic cases and epidemics of dysentery all over Denmark and partly in an endemic in an institution for the feebleminded. Bojlén employs a classification of dysentery bacilli into four groups (Shiga-Kruse, Flexner, Sonne and Schmitz). This classification is made possible by the fermentation reactions with mannite, lactose and dulcite. A finer classification within each group is possible only by means of serologic reactions. In the group of the Sonne bacilli, the capacity or the incapacity to ferment xylose proved constant, while the ability to ferment maltose was subject to change in the course of time. The employment of various sugars permitted a separation into six biochemically well defined types. The Flexner strains could be divided into ten biochemically constant types, the ability of which to ferment sorbite and saccharose was stable; the others showed changes in the course of artificial cultivation. Before the work of Bojlén was undertaken, the clinical as well as the bacteriologic diagnosis of dysentery in Denmark was rare. The epidemiological result of his work has been to show that dysentery is a common infectious disease in Denmark. In about 2.7 per cent of the cases chronic colitis develops. The results of sanitary measures in combating the disease in closed institutions and among the general population are extremely illuminating. The work includes a clear and exhaustive historical review of the development of knowledge of the bacteriology of the dysentery bacilli and of the epidemiology of dysentery, with a lengthy bibliography.

DAVIDSOHN, Chicago. [ARCH. PATH.]

Chronic Infections

TUBERCULOSIS OF THE MAJOR BRONCHI. HERBERT S. REICHLE and THOMAS T. FROST, Am. J. Path. **10**:651 (Sept.) 1934.

Tuberculosis of the major bronchi can be classified on the basis of pathogenesis as (1) infection by implantation, (2) infection by contiguity and (3) infection by continuity. The first type is decidedly less common than the other two, a fact that may be ascribed to the protective influence of cilia, mucus and bronchial peristalsis. Infection by contiguity is liable to occur because of the proximity of the extracartilaginous mucous glands to diseased lymphatics and lymph nodes. Proliferation of the adventitia and atrophy of the mucous glands tend to close this avenue. Infection by continuity occurs secondarily to implantation tuberculosis in the lower lobes and in the bronchi draining a tuberculous cavity. The major bronchi appear to be especially resistant to tuberculosis; however, when fibrosis has transformed them into rigid tubes and the mucosa and submucosa are destroyed and replaced by tuberculous granulation tissue an open focus of disease is created which is rarely closed either by natural processes of healing or by pneumothorax or thoracoplasty. We therefore suggest that the critical aspect of a tuberculous cavity lies not so much in its size per se or in the density of its wall as in its relation to a major bronchus.

AUTHORS' SUMMARY.

THE EFFECT OF MODERATELY LARGE DOSES OF VIOSTEROL ON TUBERCULOUS CHILDREN. H. G. PONCHER and B. M. GASUL, Am. Rev. Tuberc. **30**:358 (Sept.) 1934.

The fifty-nine children chosen for this experiment had all been in contact with tuberculous persons and had positive tuberclin reactions. In addition eleven showed definite parenchymatous pulmonary tuberculosis; the rest had calcified lymph nodes,

Gohn tubercles, enlarged, noncalcified lymph nodes at the hilus or no roentgenographic evidence of tuberculosis. After preliminary study, the children were given 150 drops of viosterol daily for four months, after which the dose was increased to 300 drops daily for a further period of three months. During administration of the smaller dose there was slight increase in weight. After the large dose was given, 50 per cent of the patients lost weight, and only 30 per cent showed slight or moderate gain in weight. The authors were unable to produce hypercalcemia in a period of eight months with the doses given. The effect of the administration of viosterol in large dosage to tuberculous children appears to be unfavorable. This conclusion, however, does not apply to amounts necessary for the vitamin requirements of patients.

EUGENE SMITH, Ogden, Utah.

CONGENITAL SYPHILIS: CONSIDERATION OF PREMATURITY AS AN ETIOLOGICAL FACTOR IN NEONATAL MORTALITY, PATHOLOGY, X-RAY AND TREATMENT. HARRY R. LITCHFIELD, Arch. Pediat. **51**:654 (Oct.) 1934.

Not abstracted.

WADDELL JR., University, Va.

THE LEUCOCYTE PICTURE OF THE BLOOD IN CASES OF PULMONARY TUBERCULOSIS, WITH A SPECIAL STUDY OF THE FILAMENT-NONFILAMENT COUNT. WINFIELD O. KELLEY, Bull. Johns Hopkins Hosp. **55**:171 (Sept.) 1934.

In a series of one hundred and eleven cases of pulmonary tuberculosis (in adults) in which repeated leukocyte counts were made it was noted that any single count is sufficiently accurate to be reliable.

The information obtained from a leukocyte count is of definite value in determining the clinical condition of a patient and in deciding the mode of treatment.

Tuberculous complications and other superimposed infections influence the blood picture to a great extent, and they therefore must be ruled out before an interpretation is given.

Since the leukocyte count is a sensitive indicator and since it reflects the status of the tuberculous lesion accurately, repeated counts become valuable in detecting relapses in their earliest stage.

The filament-nonfilament count, as applied in cases of pulmonary tuberculosis, has been reported for the first time in this paper. It has, therefore, been necessary to establish our own base-line for these cells, which has been placed at 960, or 16 per cent of the neutrophils. When the number of nonfilament cells exceeds this value, it is nearly always an indication of sepsis, and sometimes this count yields information that cannot be obtained by any other laboratory test.

AUTHOR'S SUMMARY.

SKIN SENSITIVENESS TO TUBERCULIN IN PRIMARY TUBERCULOSIS. C. A. STEWART, J. A. M. A. **103**:166 (July 21) 1934.

The distribution of various degrees of cutaneous sensitiveness to old tuberculin for a group of infected children with normal or inconclusive roentgenographic findings was found to be about the same as that for children with distinct, demonstrable intrathoracic lesions deemed characteristic of tuberculosis of first infection. One is, therefore, not justified in entertaining the suspicion that children with large, intense Mantoux reactions have more extensive pathologic changes or more active primary tuberculous lesions than children less sensitive to tuberculin. Apparently, soon after the initial invasion of the tubercle bacilli and before the primary lesions have time to resolve, allergy reaches an average level for the group that is sustained throughout the first few years after the primary infection.

BONAR, Salt Lake City.

THE MATERNAL TRANSMISSION OF VACCINIAL IMMUNITY IN SWINE. J. B. NELSON, J. Exper. Med. **60**:287, 1934.

The protective substances produced by vaccinia virus in swine were transmitted repeatedly to the young by way of the colostrum of the sow. In two instances immunity acquired by suckling was demonstrable in the young of six successive farrowings, which numbered thirty-seven and fifty-seven pigs, respectively. The immunity acquired by suckling began to decline during the second month and was practically negligible by the end of the third month. Vaccinia virus introduced cutaneously during the first few days of life in the passively protected pigs exerted little or no immunizing effect.

FROM THE AUTHOR'S SUMMARY.

HUGE TENSION CAVITY IN PRIMARY PULMONARY TUBERCULOSIS IN AN INFANT. S. SANES and F. E. KENNY, J. Pediat. **5**:51 (July) 1934.

A case of pulmonary tuberculosis in a 10 month old Negro infant is reported because of the unusual pathologic features—extensive cavitation, bronchogenic spread and absence of miliary dissemination. The author states that this is the first case of a tension cavity to be reported in an infant. The literature on cavernous pulmonary tuberculosis in infancy is summarized.

LEMASTER, Evanston, Ill.

SOME ASPECTS OF TUBERCULOUS MENINGITIS AND THE POSSIBILITY OF ITS PREVENTION. ARVID WALLGREN, J. Pediat. **5**:291 (Sept.) 1934.

The author discusses means by which the incidence of tuberculous meningitis may be reduced. It is shown that meningitis most frequently follows in a short time the onset of the primary tuberculous infection. It is also shown that the frequency of occurrence of meningitis is highest during the first three years of life. According to the experience of the author tuberculous meningitis can to a certain extent be prevented by avoiding tuberculous infection in infants and small children and by giving the best possible opportunity for recovery to the children already freshly infected.

LEMASTER, Evanston, Ill.

PROTECTIVE INOCULATION AGAINST TUBERCULOSIS IN INFANTS BY THE USE OF HEAT-KILLED HUMAN TUBERCLE BACILLI. T. CAMPBELL GOODWIN and FRANCIS F. SCHWENTKER, J. Pediat. **5**:475 (Oct.) 1934.

This report is a statement of the method and a record of the progress of a study in which seventy-three new-born infants of families in which tuberculous infection was present received injections of heat-killed human tubercle bacilli. The authors do not draw definite conclusions, but they believe that the results of their investigations warrant further study. The reaction to the tuberculin test became positive from three to thirteen weeks after the injection of the vaccine. In 12 per cent of the cases sterile cold abscesses developed at the site of inoculation. There was only one death from tuberculosis in this group.

LEMASTER, Evanston, Ill.

WHAT DOES A PRIMARY TUBERCULOUS INFECTION PREVENT? CHESTER A. STEWART, Nebraska M. J. **19**:321 (Sept.) 1934.

The primary infection of tuberculosis in childhood as a rule is mild. Its importance lies in that it provides the prerequisite for more serious developments later. Dissemination of the tubercle bacillus more widely throughout the body than was formerly realized is apparently proved by experiments on animals. This is probably true also in children. This primary infection makes possible rather than prevents the adult type of tuberculosis. A negative reaction to tuberculin is superior to a positive, and in the near future an initial infection will be accepted as hazardous rather than as protective.

HAMILTON, Omaha.

ANTITUBERCULOSIS VACCINATION. S. A. PETROFF, New England J. Med. **211**:677 (Oct. 11) 1934.

Of the methods of vaccination against tuberculosis which from time to time have been recommended the following three demand attention: vaccination with virulent living tubercle bacilli, avirulent living tubercle bacilli and heat-killed virulent tubercle bacilli. The author discusses thoroughly the methods used in each form of vaccination and the results obtained by their advocates. He also discusses his studies with B C G, which have been published. He believes that vaccination with living virulent organisms is out of the question as one does not care to pay the price of a possible infection to obtain a small degree of protection. Avirulent living organisms, when first introduced into the body, may not be disease-producing, but there is no assurance that once such an organism enters the body it will not become virulent, producing clinical disease. Recent experiments have shown that vaccination with heat-killed tubercle bacilli can establish protection against tuberculosis. Such vaccination is not dangerous because the organisms cannot propagate in the human body.

GENGENBACH, Denver.

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HEREDITARY SYPHILIS, WITH A CASE OF JUVENILE PARESIS. GASTON LOIGNON, Union méd. du Canada **63**:898 (Aug.) 1934.

Loignon's conception of hereditary syphilis is based on the theory that the disease may have its origin in (1) the ovum, (2) the sperm or (3) both the maternal and the paternal element. The various clinical forms depend on when the disease strikes the product of conception and can be divided into (1) syphilis of the embryo, producing abortion before the fifth month of pregnancy; (2) fetal syphilis, producing hydramnios, miscarriage or premature birth; (3) syphilis of the newborn, with cutaneous and visceral lesions; (4) infantile syphilis, which appears from the second to the sixth week of life, rarely after the fourth month, and which causes lesions in the skin, viscera, central nervous system, eyes and skeleton; (5) late hereditary syphilis, which appears during late infancy, adolescence or even in adult life and which is accompanied by mental changes that are dependent on the age of the victim, and (6) monsters of various kinds.

A case of juvenile paresis is presented in a boy of 16 years, who was treated with malaria. He was apparently normal until the age of 13, when he began having convulsions, which increased in number and severity. Following treatment the convulsions ceased, and his general condition improved. There was still some difficulty in gait three months later, but he was beginning to interest himself in his surroundings and was much more tractable in his behavior.

DAFFINEE, Boston.

CONTRIBUTION TO A COMPARATIVE STUDY OF THE TUBERCULIN TESTS IN INFANTS AND CHILDREN. G. GREGORY KAYNE and B. WEILL-HALLÉ, Brit. M. J. **2**:464 (Sept. 8) 1934.

A statistical and discursive study is made of the comparative values of the various tuberculin tests. It is suggested that the Pirquet test, because of its simplicity and ease, should be made first and if the reaction is negative the Mantoux test should be performed.

ROYSTER, University, Va.

HEALED (CALCIFIED) MILIARY TUBERCULOSIS OF THE LUNGS. DONALD PATERSON, Proc. Roy. Soc. Med. **27**:1333 (Aug.) 1934.

A girl, aged 8½ years, attended the clinic in April 1934 because she had had a cold with fever and cough about three weeks before and again three days before the visit to the hospital. Two near relatives had died of pulmonary tuberculosis. The Mantoux reaction was positive. Only a few scattered rhonchi were heard on examination. The roentgenogram showed round calcified foci of various sizes and densities scattered through both lungs. The author believes that this case is

an instance of what may be regarded as a form of hematogenous spread intermediate between the extreme of the primary focus, on the one hand, and that of miliary tuberculosis of the lungs, on the other. He concludes his report by a short discussion of the existence of such forms as that described in this case.

WILLIAMSON, New Orleans.

RECOVERY FROM TUBERCULOUS MENINGITIS IN NURSLINGS. PIERRE RUEDA, Arch. de méd. d. enf. **37**:577 (Oct.) 1934.

The author, after wide experience in the pediatric wards of the University Medical School of Rosario (the Argentine Republic) and in his private clinic, admits that recovery from tuberculous meningitis usually predicates an error in diagnosis. He is convinced, however, that numerous bona fide cases have been reported, and he has been fortunate enough to find considerable material for intensive study of the incipient stage. The customary clinical procedures do not permit sufficiently early diagnosis to be of value in the conduct of treatment. The cutaneous reaction alone is of value in estimating the potential danger, and the systematic use of this test by all practitioners would furnish an invaluable aid in prophylactic treatments. The observations of Rueda lead him to conclude that the toxins of tuberculosis have special affinity for the axis-cylinders, unprotected with myelin as they are, and that when symptoms of irritation appear it is too late to develop an adequate plan of attack.

The investigations of Arloing, Martin and others have shown that considerable time must elapse between the invasion of the bacilli and the formation of tubercles. It is in this period, Calmette observed, that the infected organism utilizes its defensive forces and its powers of elimination. If a plan could be developed of assisting the body at this critical stage, the perivascular granulations might be prevented and the toxemia correspondingly reduced. Examination of the cerebrospinal fluid of infants with positive cutireactions shows, through cytologic, chemical, bacteriologic and physical changes, the earliest involvement of the central nervous system, and the original work of the writer has been entirely in this direction. He believes that all patients showing the primary invasion, particularly when living in a contaminated milieu, are in imminent danger of involvement of the meninges and should be frequently subjected to this examination. When abnormal elements are found, intensive therapeutic measures are instituted and opportunities for further infection eliminated. Mention is made of the intraspinal injection of oxygen, proposed by Romand and François and of high voltage roentgen therapy advocated by von Bokay. The histories in fourteen cases are offered for study.

AMESSE, Denver.

THE WELL NOURISHED INFANT WITH SYPHILIS. E. LESNÉ and A. LINOSSIER-ARDOIN, Nourrisson **22**:273 (Sept.) 1934.

Congenital syphilis usually connotes a definite picture of sores involving the skin and the mucous membranes, diseased bones and general debility. In recent years, especially since the introduction of the arsenicals, a different picture is often seen. If the mother has been given modern antisyphilitic treatment during pregnancy, she may, and frequently does, bear a healthy-looking child. Many of these babies are free from taint of syphilis. Some may appear healthy until an acute infection awakens a latent syphilitic infection. In all cases of sudden death of infants, congenital syphilis should be suspected.

Children of parents known to have syphilis should be carefully observed for many years, and serologic tests should be performed when signs or symptoms suggesting congenital syphilis appear.

MCCLELLAND, Cleveland.

CRITERIA OF DIAGNOSIS OF CONGENITAL SYPHILIS IN THE NEW-BORN. PIGEAND and BROCHIER, Nourrisson **22**:277 (Sept.) 1934.

Wegner's sign (thickening of the epiphyseal line) and the Wassermann reaction furnish the most reliable diagnostic aids in the diagnosis of congenital syphilis.

That neither is infallible is shown in four cases cited. In all the instances the Wassermann reaction of the maternal blood was negative, and in one the Wegner sign was absent; yet at necropsy the spirochetes could be demonstrated in sections from the liver in all four cases and from the heart as well in one.

McCLELLAND, Cleveland.

VALUE OF THE MORO-HAMBURGER TUBERCULIN REACTION. L. BERNARD, M. LARNY and M. LENCZNER, Nourrisson **22**:280 (Sept.) 1934.

The Moro-Hamburger test is performed by rubbing a strong ointment made from old tuberculin into the skin, which has previously been prepared with ether Details for the preparation of the ointment and the technic of application are given. It is concluded that the Moro-Hamburger test is more sensitive than the original Pirquet test but less reliable than the intracutaneous test of Mantoux.

McCLELLAND, Cleveland.

THE METHOD OF LÖWENSTEIN AND ITS CONSEQUENCES. HUMANN, Progrès méd., no. 44, Nov. 3, 1934, p. 1711.

The author studied with Löwenstein in Vienna and describes his method of culturing the tubercle bacillus from the blood. He is particularly impressed with the high percentage of positive blood cultures in cases of acute rheumatic fever and believes that this result and the fact that the exudate is serous rather than purulent are strong evidence that the tubercle bacillus and not Streptococcus is the etiologic agent. The method of culture used by Löwenstein may bring light on other conditions also of which the etiology is obscure.

LESLIE, Evanston, Ill.

VARIATIONS IN THE CHOLESTEROL CONTENT OF THE BLOOD IN CHILDREN WITH PULMONARY TUBERCULOSIS AFTER SOJOURN AT A HIGH ALTITUDE. A. FOA and E. RE, Riv. di clin. pediat. **32**:1052 (Sept.) 1934.

Rabbeno at Col d' Olen first noted the increased cholesterol content of the blood at high altitudes (1927). Subsequently, other investigators have confirmed his findings.

The observations of the authors were made at a sanatorium for children in Sondrio, Italy, at an altitude of 1,250 meters above sea level. Determinations of the cholesterol content of the blood were made on the admission of the child and at monthly intervals for three months. Observations were made on twenty children with pulmonary tuberculosis.

The mean amount of cholesterol in the blood on admission to the sanatorium was 1.37 Gm. per thousand cubic centimeters; after one month it was 1.82 Gm.; after two months, 2.09 Gm., and after three months, 2.59 Gm. In only one child was there diminution in the amount following admission to the sanatorium; there was, however, a subsequent return to the value at the time of admission in this case. Several children showed little or no change in the cholesterol content of the blood during the first month.

The increase in the amount of cholesterol seems to parallel an increase in weight but not necessarily an improvement in the tuberculous process. Large increases in the cholesterol content of the blood were noticed in children showing marked clinical improvement after pneumothorax.

The authors express the belief that the mechanism of the effect of altitude on cholesteremia is through the neuro-endocrine system, especially the adrenal glands.

HIGGINS, Boston.

PULMONARY TUBERCULOSIS—NEW ORIENTATIONS IN ITS STUDY. L. ALCALDE NOY, An. de pediat. **1**:296 (May) 1934.

The primary infection of tuberculosis that produces a positive Pirquet reaction does not prevent the development of subsequent pulmonary tuberculosis.

In eighty-four patients with tuberculosis (cited from Steward) who had primary lesions at the first examination, thirty-six, or 43 per cent, showed other lesions during the first ten years of life, and twenty-five or 30 per cent, had reinfection following primary tuberculosis when first seen. Such allergy as is seen does not insure protection against subsequent tuberculous infection. The author's conclusions are:

Primary pulmonary tuberculosis is revealed in the roentgenogram as parenchymatous infiltrations, calcified ganglions and Ghon tubercles. These lesions represent simply different phases of development of the same clinical condition of primary tuberculosis or infantile tuberculosis. The general tendency of these primary lesions is to resolve and end in calcification. The human body is able to destroy or dissolve a pulmonary infection known as a primary complex only one time. Reduced to calcified rests this primary lesion is not able to react again and produce the adult type of pulmonary tuberculosis. Death occurs rarely from this primary infection. The prognosis is excellent if reinfection is avoided. Primary pulmonary tuberculosis produces various symptoms which disappear over the course of few or many weeks. From this moment and for the rest of the life of the patient these primary lesions do not produce any more clinical symptoms, and only occasionally does a very large Ghon tubercle act as a foreign body and erode a vein, producing hemoptysis. Pulmonary tuberculosis in consequence is not a development from a primary lesion, but develops from a reinfection in a person who has had a primary lesion. The reinfection responsible for the pulmonary tuberculosis is in all probability in the majority of cases of exogenous origin. The lesions of reinfection appear habitually in the apexes of the lungs. These lesions are able to exist for months and years without producing any clinical symptoms or physical signs. These previously inactive characteristics develop in children from 13 to 19 years of age, frequently producing cavities, and may produce death. In the adult type of tuberculosis calcification is rare. Puberty appears to favor the apparent awakening of the existing inactive pulmonary lesion, producing the subapical adult type of tuberculosis. This adult form of tuberculosis has a tendency to progress and produce cavities, while the primary tuberculosis has the tendency to calcify and recede. The prognosis is always grave in the adult form of tuberculosis and frequently ends in death, whereas death rarely occurs in the primary type of tuberculosis. The author repeats that the adult form of tuberculosis is a new invasion of the tubercle bacillus and does not develop from the primary focus of infection.

HERRON, Spokane, Wash.

TUBERCULOUS MENINGITIS IN INFANCY. LUIZ DE FARIA, Arch. de pediat., Rio de Janeiro **6**:981 (Sept.) 1934.

This article discusses in full the frequency of occurrence, age incidence, pathologic anatomy, symptoms, special diagnostic signs and laboratory tests for tuberculous meningitis. A full bibliography of foreign articles is given.

SANFORD, Chicago.

DIAGNOSIS OF TUBERCULOSIS IN INFANTS. GEORGES GUIMARES, Arch. de pediat., Rio de Janeiro **6**:1015 (Sept.) 1934.

The diagnosis of tuberculosis in infants should be based on the following: (1) clinical examination, with a history of contact and the typical manifestations; (2) reactions to the tuberculin tests, such as cutireaction and the percutaneous, intradermal and subcutaneous reactions; (3) roentgenographic examination, including a series of roentgenograms if necessary; (4) determination of the presence of the Koch bacillus by direct examination and by indirect culture or inoculation of animals.

SANFORD, Chicago.

CHILDREN OF PARENTS WITH DEMENTIA PARALYTICA. M. SCHACHTER, Med. de los niños **35**:257 (Sept.) 1934.

Children of parents with dementia paralytica have many neuropsychic disturbances. There is gradual deterioration when they reach the age of from 12 to 13 years. Some may appear to be above the normal intellectual level, but in the great majority of cases mental deterioration develops. In some of these children dementia paralytica develops as in their parents; therefore they should be studied and treated.

DWYER, Kansas City, Mo.

THE TUBERCULIN SKIN TEST OF LOEWENSTEIN. C. SAINZ DE LOS TERREROS, Rev. san. e hig. pub., vol. 8, no. 2, Feb. 1933.

The test is performed in the same way as the Pirquet test and is evidently the same. In tests on 1,002 school children, 545 of whom were boys and 457 girls, the authors obtained the following results: a negative reaction for 227, or 42 per cent, of the boys and 238, or 52 per cent, of the girls; a feebly positive reaction for 147, or 27 per cent, of the boys and 91, or 19 per cent, of the girls; a definitely positive reaction for 94, or 17 per cent, of the boys and 66, or 15 per cent, of the girls; an intensely positive reaction for 76, or 13 per cent, of the boys and 55, or 12 per cent, of the girls, and a very severe reaction for 1 boy and 7, or 1.5 per cent, of the girls. The age incidence in the positive cases was as follows: 5 years, 30 cases; 6, 27 cases; 7, 34 cases; 8, 56 cases; 9, 75 cases; 10, 104 cases; 11, 89 cases; 12, 56 cases; 13, 50 cases, and 14, 8 cases.

HERRON, Spokane, Wash.

TRANSPLACENTAL TRANSMISSION OF TUBERCULOSIS. N. PALACIOS COSTA and M. FALSÍA, Rev. Soc. argent. de biol. **10**:207 (Aug.) 1934.

The work of Fontes and many others has established the undamaged passage of the ultravirus of tuberculosis through the placenta to the fetus. This ultramicroscopic filtrable tuberculous virus when inoculated into animals produces hypertrophy of the lymphatic glands, and the Koch bacillus was noted in these glands on sectioning. The virus produces the same pathologic changes as the bacillus does. Mönckeberg and Vergarak, in 1923, took 2 or 3 cc. of blood from the umbilical cords of new-born infants of tuberculous mothers and injected this blood intramuscularly into twelve guinea-pigs. Four positive results were observed. The guinea-pigs were killed one month later, and in the cases with positive results glandular hypertrophy and caseation were found in the region draining the area of the inoculation. Of the babies from whom the blood had been obtained in these four cases, three died a few hours after birth, and on autopsy no tuberculous lesions were observed. These investigators concluded that tuberculosis can be transmitted by the direct passage of the Koch bacillus through the placenta, but that this is not common (three cases of twenty-six), whereas the transplantation of tuberculosis by the ultravirus through the placenta is much more common and occurs generally between the third and sixth month of intra-uterine life. In 1929, these authors obtained positive results in thirty-eight of one hundred guinea-pigs inoculated with blood from the umbilical cords of infants of tuberculous mothers.

Palacios Costa and Falsía took 10 cc. of amniotic fluid from twenty-four tuberculous mothers pregnant for more than six months and injected 5 cc. into each of two guinea-pigs, which were killed after two and four months. They obtained positive results in three cases (12.5 per cent). When emulsions of twenty-one placentas from tuberculous mothers were injected into guinea-pigs, a positive result was obtained in only one case (4.76 per cent). They concluded that tuberculous infection of the amniotic fluid without involvement of the placenta is possible and vice versa. All the three infants born with the amniotic fluid that showed positive results were separated from their mothers and developed normally.

HERRON, Spokane, Wash.

Internal Diseases

THERAPEUTIC VALUE AND EFFECTS OF AMNIOTIN IN GONORRHEAL VAGINITIS IN CHILDREN. J. HUBERMAN and H. ISRAELOFF, J. A. M. A. **103**:18 (July 7) 1934.

In this investigation the estrogenic preparation amniotin was used solely in doses of 100 rat units hypodermically three times a week. The preparation had no cumulative action, and no local or constitutional reactions were noted in the six patients treated. The renal threshold of amniotin was found to vary with the patient, and the amount of the estrogenic substance found in the urine was directly proportional to the intensity of the treatment. Increase in the number of epithelial layers of the vaginal mucous membrane is not the sole factor responsible for eradication of gonorrheal vaginitis. The most important aid is the formation of a cornified layer of epithelial cells which forms a barrier against reinfection. The method is safe, and involution of the vaginal structures occurs when treatment is stopped. Hospitalization is unnecessary.

BONAR, Salt Lake City.

UNDESCENDED TESTES IN MAN AND RHESUS MONKEYS. S. B. D. ABERLE and R. H. JENKINS, J. A. M. A. **103**:314 (Aug. 4) 1934.

Up to the present there have been two methods of handling cryptorchism. One is to wait for spontaneous descent, which has certain disadvantages, of which the possibility of abnormal development is important. The other method is surgical placement of the testes in the sac, a method which does not always have a successful termination. Recently a third possibility has been presented, namely, the administration of the anterior pituitary-like principle from the urine of pregnancy. Injections of this principle caused the testes to descend in two of four of the authors' cases. In only one case was descent complete. Hypertrophy of the scrotum and testes occurred, and in one case there was increased growth of the penis. In immature monkeys with unilateral orchidectomy, this hormone caused incomplete descent of the testes in one animal and partial descent in four, in all of which the fascia surrounding the vas deferens and spermatic vessels was too short to allow further descent. The failure of the treatment may have been the result of an incorrect amount of the hormone, age, nutrition or some other endocrine factor. In man mechanical obstruction and developmental irregularities must be considered. The testes of the patients given injections showed marked tubular enlargement and corresponding increase of interstitial tissue, but no mature sperm. Identical amounts of the hormone caused various degrees of hypertrophy in the prostate, seminal vesicles and testes of immature monkeys. The total dose of the hormone does not bear a direct relation to the distance of the descent of the testes either in man or in monkeys.

BONAR, Salt Lake City.

ENDOCRINE DWARFISM. W. ENGELBACH and R. L. SCHAEFER, J. A. M. A. **103**:464 (Aug. 18) 1934.

Since 50 per cent of the total growth is attained by the third year, it logically follows that diagnosis and adequate treatment of dwarfism during the infantile and early juvenile periods should give greater therapeutic results. Evidence points to the fact that somatic growth is produced by the eosinophilic cell of the anterior lobe of the hypophysis, which means that every structure of the body, from an individual cell to the constitutional whole, is involved. Seven patients were given intramuscular injections of 2 cc. of a growth-promoting anterior pituitary hormone (antuitrin G) three times a week. No alteration in the diet was made. In the gross the histories of these patients suggested a stationary or minimal growth, and during a control period practically no increase in height was noted. These studies led to the conclusion that the extract employed does not contain a growth hormone, and that thyroid extract is a valuable adjunct in this form of treatment. The cases with the most favorable response were those in which there was a delay in osseous development. Sex maturity and epiphyseal closure preclude stimulation of statural growth.

BONAR, Salt Lake City.

ON THE REAGIN CONTENT OF BLISTER FLUID. W. C. SPAIN and JOHN M. NEWELL, J. Allergy **5**:331 (May) 1934.

Blisters were formed on the skin of persons sensitive to ragweed, timothy, house dust, horse epithelium and rabbit epithelium by the cantharides method. Dilutions of the blister fluid and of blood serum were injected into the skin of normal persons, with the usual passive transfer procedure. The sites were tested twenty-four hours later with the ragweed, timothy, horse epithelium or rabbit epithelium. The reaction at the site where the blister fluid was used was just slightly less than that at the site where the serum was used. This would indicate that the reagin content of the blister fluid is comparable to that of the corresponding serum.

An unrelated protein, cottonseed extract, was used in another group of experiments to show the specificity of the antibodies in the blister fluid. There was no reaction at the site where the cottonseed extract was used, although there was a marked reaction when the specific protein was used.

These experiments would indicate that specific antibodies occur in the blister fluid as well as in the serum of hypersensitive persons. HOYER, Cincinnati.

THE DIAGNOSTIC IMPORTANCE OF THE HETEROPHILE ANTIBODY TEST IN LEUKEMIA. ALAN BERNSTEIN, J. Clin. Investigation **13**:685 (July) 1934.

Heterophile agglutinins (for sheep's red blood cells) in the blood serums of twenty-one patients with leukemia were confined to low titers: less than 1:4 in twenty instances. In most of the conditions simulating leukemia, heterophile agglutinins were found in higher titers, up to 1:16. The intravenous administration of horse serum, which in normal persons elicits an increase in the serum heterophile antibodies, failed to raise the serum heterophile antibody titer in one case of lymphoid leukemia. Two clinical histories are given of patients whose heterophile agglutinin titer was of assistance in differential diagnosis.

GUEST, Cincinnati.

CONCERNING HEREDITY IN DIABETES. ADRIEN BLEYER, J. Missouri M. A. **31**:325 (Aug.) 1934.

The case of a diabetic child in a diabetic family is reviewed as further evidence in favor of the inheritance of diabetes. This child who was oversize and overweight, with a distribution of fat indicating abnormality of the posterior lobe of the pituitary, became diabetic at the age of 10 years. The mother, who is obese, became diabetic when the child was 13, and the father when she was 14. It is suggested that when sugar is found in the child's urine it might be advantageous to make a blood sugar test on the blood relatives, particularly the parents.

BERGER, Kansas City, Mo.

LYMPHATIC LEUCEMIA RESEMBLING RHEUMATIC FEVER IN A CHILD. LUCY PORTER SUTTON, J. Pediat. **5**:61 (July) 1934.

A 3 year old white child with lymphatic leukemia had as outstanding symptoms irregular fever and pain in the joints. The blood picture was typical. The spleen, liver and lymph nodes became enlarged, and the bones showed extensive rarefaction in the roentgenograms. An autopsy was not done.

LEMASTER, Evanston, Ill.

HEART DISEASE AMONG CHILDREN OF SCHOOL AGE. J. V. DE PORTE, New York State J. Med. **34**:448 (May 15) 1934.

Since 75 per cent of all heart disease develops in children under 10 years of age, examination of the hearts of school children is very important.

Eighty-six thousand children were examined in the schools of cities and villages of New York. An incidence rate for heart disease of 5 per thousand was

found. Figures are given for 634 cases. In 302 of these the condition was due to rheumatic infections, and in 40 it was of congenital origin. Disease of the mitral valve was found in 446 cases, and disease of the aortic valve in 23 cases.

AIKMAN, Rochester, N. Y.

ABDOMINAL PAIN IN CHILDREN. EDWARD SHERRARD RIMER, New York State J. Med. **34**:456 (May 15) 1934.

An outline is presented for the study of abdominal pain. Allergy as a cause of pain is discussed.

AIKMAN, Rochester, N. Y.

THE CONTINUOUS INTRAVENOUS METHOD OF FLUID ADMINISTRATION (VENOCLYSIS) IN PEDIATRICS. SAMUEL KARELITZ, New York State J. Med. **34**:631 (July 15) 1934.

Karelitz gives an excellent description of the use of venoclysis as practiced at Mount Sinai Hospital in New York. Eighty-eight patients with severe cases of alimentary intoxication and twelve with mild cases were so treated. Seventy-five other patients were also treated, including patients with cyclic vomiting, diabetic coma, acute nephritis, bacteremia, streptococcic peritonitis, extensive burns, pyloric stenosis and other conditions in which reduction of fluid had caused circulatory collapse. Excellent results were obtained, and the author believes that this is the method of choice when replacement of fluid is required. Local occlusion of veins occurred in 25 per cent of the cases after from ten to ninety-six hours. Thrombophlebitis was seen in four cases. Visible edema was observed in some cases. In a few considerable fluid was noted at autopsy in the peritoneal cavity, and edema of the tissues, including the brain, was also present.

AIKMAN, Rochester, N. Y.

ULCERATIVE COLITIS: I. THE RELATIONSHIP BETWEEN BACILLARY DYSENTERY AND ULCERATIVE COLITIS. THOMAS T. MACKIE and MARY S. B. GAILLARD, South. M. J. **27**:492 (June) 1934.

In 42 per cent of eighty-three unselected consecutive cases of chronic ulcerative colitis in New York City cultural or serologic evidence of bacillary dysentery was present. Dysentery bacilli were recovered from 20.4 per cent of the patients. Similar evidence of infection by Bacillus dysenteriae was found in nine of one hundred and two control cases, in six of which there was a history suggestive of mild clinical bacillary infection. The evidence available does not support the contention of the unitary bacteriologic etiology of ulcerative colitis.

SCHLUTZ, Chicago.

A CASE OF IMPERFORATE HYMEN IN WHICH GENERALIZED PERITONITIS DEVELOPED. LEON GERIN-LAJOIE, Union méd. du Canada **43**:468 (May) 1934.

An 18 year old girl was sent to the hospital because of diffuse abdominal pain and vomiting of about a month's duration. The week before entry she had noticed a bloody discharge from the vagina. She had never menstruated. She was in very poor condition, with some spasm in the right iliac fossa. The hymen had a very small tear. The vagina contained a large clot of blood. Laparotomy was performed and purulent, fetid fluid under pressure was discovered. The patient died the same night. Autopsy showed generalized peritonitis, pericystitis, pulmonary congestion, distention and gangrene of the vaginal mucosa and the uterus.

The author makes a plea that routine examination of the genitalia of adolescent girls be made, especially when there is a history of amenorrhea or recurrent monthly attacks of abdominal pain.

DAFFINEE, Boston.

FIVE CASES OF CONGENITAL LUNG CYST. G. B. FLEMING, Arch. Dis. Childhood **9**: 201 (Aug.) 1934.

Five cases of single cyst of the lung are described. In four cases the cysts contained air, while in one there was fluid. In three of the cases there were physical signs of pneumothorax. The cyst in one case was lined by columnar ciliated epithelium and in another by flattened epithelium. Ciliated epithelial cells were detected in the fluid withdrawn from the fluid-containing cyst. Three of the patients died; two are alive and apparently well. In two of the cases in which there were signs of respiratory embarrassment paracentesis and withdrawal of air brought temporary relief.

KELLY, Milwaukee.

THE AFTER HISTORY OF CASES OF PLEURISY WITH SEROUS EFFUSION IN CHILDREN. D. W. SMITHERS, Arch. Dis. Childhood **9**:245 (Aug.) 1934.

Between 1920 and 1932, seventy-one patients with pleurisy with effusion under 15 years of age were admitted to St. Thomas' Hospital. The presence of fluid was confirmed by aspiration in forty-nine cases. Thirty-two of these forty-nine patients were followed from thirteen and one-half years to one year and one month after discharge.

Of the thirty-two patients followed, twenty-five showed no evidence of subsequent tuberculosis, all being perfectly well except two who were in hospital for some other disorder. Three had vague symptoms but no definite evidence of tuberculosis; two had died of pulmonary tuberculosis; one had caries of the dorsal spine, and one had tuberculous peritonitis. Expressed in another way, it was found that 12.5 per cent subsequently contracted tuberculosis, 6.25 per cent having died of pulmonary tuberculosis; 9.4 per cent presented doubtful signs and symptoms, and 78.1 per cent remained perfectly well. Tuberculosis is a much less frequent sequela of pleural effusions in children than in adults, but occurs sufficiently often to necessitate prolonged treatment and careful supervision of these cases. The dangerous period to the child is the first four years following the effusion, particularly the first year.

KELLY, Milwaukee.

ACID METABOLISM IN RHEUMATIC CHILDREN. W. W. PAYNE, Arch. Dis. Childhood **9**:259 (Aug.) 1934.

In this investigation three groups of children were used: two hundred children attending a clinic for patients with rheumatic disease and two control groups—one being a group attending a clinic for patients with asthma and the other, a group of healthy children. Three specimens of urine (1) on rising, (2) after breakfast (3) and on going to bed, were examined for: specific gravity, p_H by means of indicators, free acid titrated to p_H 7.6 with tenth normal sodium hydroxide ammonia and titration with tenth normal hydrochloric acid to free acid, using methyl orange, chlorides, phosphate and urea.

It was concluded that the rheumatic child in a quiescent interval excretes more acid in the urine than does either an asthmatic or a normal child. This excess production of acid is insufficient to disturb the equilibrium of the blood. It is suggested that there is some truth in the "acid diathesis" theory of rheumatism.

KELLY, Milwaukee.

HELMINTHIASIS IN CHILDREN. P. D. DAVYDOFF, Brit. J. Child. Dis. **31**:193 (July-Sept.) 1934.

This report is from the North Caucasus State Institute for the Protection of Maternity and Childhood. The first part of the article consists of a description of the helminths most frequently found in children. These include Oxyuris vermicularis, Ascaris lumbricoides, Trichocephalus trichiura, Hymenolepis nana, Dibothriocephalus latus and a few others, the first three being by far the most prevalent.

"The injurious effects of helminths on children are of various kinds; they consist principally in pernicious anemia, emaciation, nervousness, gastrointestinal disorders and invasion of the internal organs, such as the liver, lungs, muscles, brain and spinal cord and toxaemia."

Oxyuris vermicularis is frequently the cause of appendicitis in children.

The most effective method of expulsion of Hymenolepis nana and Taenia solium is the introduction of male fern by the duodenal tube.

After expulsion of ascarides it is necessary to give large doses of purgatives, owing to the intoxication liable to occur on destruction of these helminths.

LANGMANN, New York.

NOCTURNAL ENURESIS. C. J. C. EARL, Brit. J. Child. Dis. **31**:205 (July-Sept.) 1934.

A few of the many factors that have been mentioned as possible causes of enuresis are discussed. The object of the essay is to stress the value of the psychologic treatment in enuresis. Ideally such treatment should be carried out by a children's psychiatrist or at a child guidance clinic. "For many reasons, however, such treatment is not always easily procured, and for the simple cases of enuresis uncomplicated by other behavior disorders, simple suggestion, superficial and symptomatic though it may be, is adequate and efficient."

LANGMANN, New York.

ENTEROGENOUS CYSTS. W. E. A. HUGHES-JONES, Brit. J. Surg. **22**:134 (July) 1934.

Enterogenous cysts may be discovered anywhere from birth to later life, and their discovery usually depends on symptoms of a mechanical nature, such as intestinal obstruction which results from stenosis, intussusception or volvulus. The cysts have been found chiefly in the small intestine, though a few have been reported in the ascending and transverse colon. As to their position, they may be in the submucosa, muscle layers or subperitoneal region or in the mesentery of the bowel.

Two theories have been advanced regarding their etiology: (*a*) that they arise from diverticula of the intestine of the embryo and (*b*) that the epithelium becomes detached from the embryonic intestine at a very early age and develops into a cyst. The treatment is operation.

SUMMERFELDT, Toronto, Canada.

DUODENAL ULCER IN A 10-YEAR-OLD CHILD. M. BRICE SMYTH, P. T. CRYMBLE and F. M. ALLEN, Brit. M. J. **1**:1074 (June 16) 1934.

The authors report a duodenal ulcer in a child 10 years of age. The clinical manifestations were intermittent pain in the region of the stomach for the past six months. The pain was present in the morning and was relieved by a hot drink. At times it persisted throughout the morning. There were tenderness under the right costal margin, gastric retention for seven hours on roentgen examination and an absence of filling of the duodenum.

ROYSTER, University, Va.

CONGENITAL HYPERTROPHIC STENOSIS OF THE PYLORUS; AN ANALYSIS OF 145 CASES TREATED BY OPERATION. H. L. WALLACE and L. B. WEVILL, Brit. M. J. **1**:1153 (June 30) 1934.

This article is a statistical analysis of one hundred and forty-five cases of this condition in which treatment was by operation.

ROYSTER, University, Va.

REFLEX ASTHMA: ITS PATHOLOGY AND TREATMENT. H. H. MOLL, Brit. M. J. **2**:299 (Aug. 18) 1934.

The mechanism of reflex asthma is discussed, and an outline of early experiments and the pathologic features is given in brief detail. A review of the clinical cases follows, while nasal symptoms are discussed at greater length. Nasal

abnormalities are likewise discussed. The results of operation and a general discussion of the treatment follows. The conclusions of the author's paper are as follows:

"In concluding, one may say that nasal symptoms often do not disclose the part which the nose is playing as an etiological factor in asthma, as they themselves may be due to an allergic reaction. The presence of nasal abnormalities in the nose and throat is of no greater help, as they are often coincidental or are also a result of the asthma.

"1. In a series of 326 cases of asthma about half the number of patients complained at one time or another of nasal symptoms. These symptoms were mostly due to vasomotor affections of the nose and not true coryzal attacks.

"2. Vasomotor affections of the nose and throat occurred in all types of sensitivity, but were definitely more common in pollen-sensitive cases of asthma.

"3. Abnormalities of the nose and throat were found in 77.9 per cent of cases, but were mostly coincidental and minor causal factors.

"4. Turbinal hypertrophy and hyperplastic sinus disease were often the result rather than the cause of the asthma, and were found slightly more frequently in protein-sensitive cases.

"5. Of 135 cases which received operative treatment, 109 cases were followed up, and of these 50.4 per cent were improved and 2.7 per cent (three cases) were cured."

ROYSTER, University, Va.

CONSTANCY OF THE DAY-TO-DAY LEUCOCYTE BLOOD COUNT. W. F. HARVEY and T. D. HAMILTON, Edinburgh M. J. **41**:465 (Aug.) 1934.

The authors entitle this a medicostatistical study and explain that the title might contain the word "variability" instead of "constancy." The numbers of the several types of leukocytes are similar from day to day, and at the same time the several counts will not be exactly alike, varying with the rate at which new cells are added or old cells destroyed. Harvey and Hamilton state that their investigation was simply to learn the day-to-day variations of blood character on a sufficient number of occasions to make them valid as statistics by which one could measure the probable type of variation in this examination. Many tables and graphs are used to present the figures obtained from the continued study of two adults, one normal and the other a subject with allergy.

NEFF, Kansas City, Mo.

VON GIERKE'S GLYCOGEN ACCUMULATION DISEASE. P. M. ANDERSON and D. G. R. VICKERY, M. J. Australia **1**:753 (June 9) 1934.

A 4 year old girl, whose case is reported by Anderson, showed marked enlargement of the liver, constant acetonuria and failure of blood sugar response after the injection of epinephrine, but her general condition seemed strikingly good in spite of the marked failure of sugar metabolism. No treatment seemed of any avail, but she was slowly improving spontaneously.

The case reported by Vickery is similar to the previous one, except that this infant had repeated convulsions and was mentally retarded.

TENNEY, Madison, Wis.

VENA AZYGOS LOBE IN A CHILD WITH CHRONIC BRONCHITIS. KENNETH HARRIS and PETER KERLEY, Proc. Roy. Soc. Med. **27**:1231 (July) 1934.

A boy of 7 years had complained of chronic winter cough for three years and showed signs of chronic bronchitis. Examination of the sputum showed no tubercle bacilli. Roentgen examination showed chronic bronchitis and emphysema and a typical vena azygos lobe, with the line curving in the usual direction. The authors discuss this condition from a clinical, roentgenologic, anatomic and etiologic standpoint.

WILLIAMSON, New Orleans.

THE HAEMOPOIETIC ACTIVITY OF THE NORMAL AND ABNORMAL HUMAN LIVER, WITH SPECIAL REFERENCE TO PERNICIOUS ANEMIA. J. F. WILKINSON and LOUIS KLEIN, Quart. J. Med. **3**:341 (July) 1934.

Wilkinson and Klein prepared extracts of liver from untreated persons with pernicious anemia, from treated persons with pernicious anemia, from four normal persons (i. e., persons not suffering from anemia) and from a patient with polycythemia rubra. The same method was employed in the preparation of all the extracts (*British Pharmacopoeia* [1932], the preparation of "Extraction Hepatis Siccum"), with slight modifications. After a suitable period of observation the various extracts were injected intramuscularly into persons with frank cases of pernicious anemia, and careful observation of the reticulocytes, the red cell count and the hemoglobin was made.

The authors concluded that the antianemic "liver principle" is definitely present in normal human livers and in livers from treated persons with pernicious anemia in active remission but is absent from the livers of untreated persons with pernicious anemia. The liver from a patient with polycythemia rubra was found to be more potent than normal human or calf liver. BRADFORD, Rochester, N. Y.

THE TREATMENT OF MUSCULAR DYSTROPHY WITH GLYCINE. D. P. CUTHBERTSON and T. K. MACLACHLAN, Quart. J. Med. **3**:411 (July) 1934.

Nine cases of muscular dystrophy were investigated as regards the response to the administration of glycine. All the patients showed a temporarily increased creatinuria as a result of the ingestion of glycine. In the majority of the cases there was some evidence of improvement in the power of some of the specific muscles affected, but this was least in the pseudohypertrophic group. Some general improvement was noted in two cases of muscular atrophy. One patient showed some increase in power of the affected muscles. The authors conclude that the term "cured" cannot be applied to the end-results. BRADFORD, Rochester, N. Y.

LUNG ABSCESS, WITH SPECIAL REFERENCE TO CAUSATION AND TREATMENT. JAMES MAXWELL, Quart. J. Med. **3**:467 (July) 1934.

This article constitutes a critical review of the subject, covering forty-eight pages and giving three hundred and eighty references. The part which deals with pulmonary complications following tonsillectomy might have a particular appeal to the clinical pediatrician. The work also contains an interesting review of the literature dealing with experimental abscess of the lung.

BRADFORD, Rochester, N. Y.

RENAL EFFICIENCY TESTING: THE UREA CONCENTRATION RANGE IN DIAGNOSIS AND PROGNOSIS OF KIDNEY INEFFICIENCY. J. D. S. CAMERON, Tr. Med.-Chir. Soc. Edinburgh, 1933-1934, p. 73; in Edinburgh M. J., June 1934.

Cameron concludes that among practical and easy tests of renal efficiency the best is Calvert's test for the urea concentration range, which is applied while the patient is asleep, when the concentrating power of the kidney is much greater. The technic is described. The subjects tested ranged from 4 years of age up to old age. In the age period up to 10 years the average minimum and maximum ranges were 0.3 and 3.8 per cent. The imminence of uremia is indicated by a decrease in the range. The prognosis as well as the diagnosis is aided. In acute nephritis the patient should not be allowed to be up until the range is normal.

NEFF, Kansas City, Mo.

BLOOD CHOLESTEROL IN DIABETES OF CHILDHOOD. P. NOBÉCOURT and PAUL DUCAS, Arch. de méd. d. enf. **37**:522 (Sept. 9) 1934.

In an endeavor to confirm the findings of American investigators (Gladys Boyd, Rabinowitch, Azel Hunt and P. White), who concluded that the level of cholesterol

in diabetes of the young was not necessarily raised, the authors made an intensive study of eight children suffering from a severe form of this disease. In this connection it was noted that, while in America the Bloor method of determining cholesteremia is employed and the normal limit set at about 2 Gm., in France the technic of Grigault is used and the average for health expressed in 1.5 Gm. The results in this research paralleled closely those of the authors cited; it would appear that there is no close relation between the cholesterol content, on the one hand, and glycemia, carbohydrate tolerance, weight and height, on the other.

AMESSE, Denver.

INITIAL PERIOD OF KALA-AZAR IN CHILDREN. RAPHAEL GUERSCHENOWITSCH, Arch. de méd. d. enf. **37**:531 (Sept.) 1934.

There has always been a question concerning the period of incubation of kala-azar in young subjects; in addition, the early clinical picture has not been clearly defined.

The author, writing from the Institute of Medicine at Taschkent, middle Asia, where the disease seems to be endemic, discusses the histories of seven patients ranging in age from 3 months to 12 years. The conclusions affirm that before the first day of fever there are a series of general prodromal symptoms which appear insidiously, such as progressive pallor, enlargement of the spleen, loss of appetite, bodily weakness and altered disposition. Following this apyretic stage comes the initial fever, during which all the symptoms of the prodromal period are exaggerated; there is transient leukocytosis preceding the characteristic leukopenia. The latter phenomenon may be considered pathognomonic, but it should be verified by puncture of the sternum or of a suitable lymphatic gland.

AMESSE, Denver.

PREVENTION OF ESOPHAGEAL STRICTURE FOLLOWING CORROSIVE BURNS. HANS SALZER, Bull. Assoc. internat. de pédiat. prevent. **2**:8, 1934.

To the old method of doing nothing to prevent esophageal strictures following burns Professor Salzer opposes the modern conception, which advocates the introduction of bougies into the esophagus soon after the accident. In his own clinical practice he has treated a great number of patients after burns by caustics, using a soft sound, which is introduced for a few minutes only during the first days and later is left in situ for as long as half an hour. He has noted no perforation except in a very few severe cases, and on one occasion he was able to observe (during an autopsy for another cause) the beneficial effects of the treatment. Professor Salzer finds this method less painful for the patient, and it has the added advantages of getting rid of the last traces of the caustic and allowing the patient to be fed in normal fashion. To prevent stricture is surely easier and better than to treat it once it exists. The new method is already employed by a number of practitioners, and Professor Salzer greatly desires to see it generalized.

AMESSE, Denver.

EXTRACTION OF A METALLIC FOREIGN BODY FROM THE RIGHT BRONCHUS UNDER ROENTGEN CONTROL. D'HALLUIN, Bull. et mém. Soc. de radiol. méd. de France **22**:261 (May) 1934.

A screw was seen to be lodged in the right bronchus of a 4 year old girl. A forceps was easily guided by means of the fluoroscope past the glottis and into the bronchus. The author has collected from the literature reports of seven other cases of extraction under fluoroscopic control, always with facility and without injury. He suggests that this method, which he regards as simpler and more efficacious than bronchoscopy, be often resorted to.

VINTON, Brooklyn.

FIFTH CHILD SUFFERING FROM GAUCHER'S DISEASE IN THE SAME FAMILY. W. WORINGER, J. de méd. de Paris **54**:689 (Aug. 9) 1934.

The first four cases of Gaucher's disease in the family were reported in 1927 in the *Revue française de pédiatrie*. The present case is that of an infant who up until 3 months of age presented no abnormality. Following this time there developed progressive enlargement of the spleen and liver, dysphagia and some rigidity of the extremities; death from cachexia occurred at the age of 9 months. Five of seven children in the family were similarly affected. No definite history of any similar condition among the older generations could be obtained.

LESLIE, Evanston, Ill.

RÔLE OF THE ENDOCRINOSYMPATHETIC FACTOR IN THE MECHANISM OF FEVER PRODUCTION. ALBERT SALMON, Presse méd. **42**:1289 (Aug. 15) 1934.

Salmon believes that the pathogenesis of fever, considered heretofore a reaction of the tuber cinereum, may be clarified by a study of the physiologic connections of the vegetative center with the adrenal and the hypophyseal glands, which secrete a substance capable of producing fever. Experimental stimulation of the tuber cinereum produces hypersecretion of epinephrine, and the functional synergy existing between the tuber cinereum and the posterior lobe of the hypophysis suggests that the production of fever by the tuber cinereum involves a hypersecretion of epinephrine and in all probability of posterior pituitary hormone also. Diabetes insipidus often disappears spontaneously during the course of a fever. The hypersecretion of epinephrine in fever explains perfectly the mechanism of chills, arterial hypertension, tachycardia and hyperglycemia; hypersecretion of the posthypophysis explains the mechanism of water retention, which constitutes one of the fundamental pathogenic elements in all fever. Hypothermia follows destruction of the posthypophysis. As the water-regulating mechanism of the hypophysis is a factor in maintaining the body temperature, the diuretic and sudorific action of most antipyretics is easily understood.

BIEKER, St. Petersburg, Fla.

RELAXATION OF THE DIAPHRAGM IN INFANCY. A. CABITTO, Clin. pediat. **16**:649 (Aug.) 1934.

Cabitto reports the case of a 25 day old infant who was brought to the clinic because of cyanosis and difficulty in breathing and was found to have a relaxation of the diaphragm. He reviews the differential diagnosis between this condition and diaphragmatic hernia without adding new facts in regard to it.

DOOLEY, New York.

THE OPSONIC INDEX IN EMPYEMA IN INFANTS. S. QUADRI, Prat. pediat. **16**:631 (Aug.) 1934.

The opsonic index was studied with the various types of Pneumococcus in seventeen cases of empyema in infants. There is a definite relationship between this index and the severity of infection, the more severe cases showing a subnormal value, with a rise in the event of a favorable outcome. Fluctuations in the index occur with improvements or relapses in the disease and furnish an indication of the prognosis and of the effect of any given course of treatment.

DOOLEY, New York.

A NEW SENSITIVE AND RAPID SERUM REACTION FOR THE DIAGNOSIS OF INFANTILE LEISHMANIASIS. L. AURICCHIO and A. CHIEFFI, Pediatria **42**:915 (Aug. 1) 1934.

This paper represents a report of work aimed at the development of a more practical and at the same time reliable method for the diagnosis of leishmaniasis in children. The authors give a detailed discussion of the theories involved and also explain their technic in detail. The report indicates that they have developed

a test which gives negative results with the blood serum of normal children and of children with diseases other than leishmaniasis, whereas in the presence of leishmaniasis they were able to obtain a positive reaction in all his cases.

SIGNORELLI, New Orleans.

STATES OF ACIDOSIS AND ALKALOSIS IN BRONCHIAL ASTHMA IN BABIES. TULLIO LUZZATTI, Ric. e. studi patologia d. Ricambio **9**:1 (Jan.-June) 1934.

Luzzatti is interested in patients with bronchial asthma in whom there is no evidence of protein sensitization. He reports the records of three infants who from early life had repeated attacks of bronchial asthma. One of these had associated acetonemia often coincidental to the attacks. Being aware of the use of alkaline therapy in intoxication and acetonemia, Luzzatti employed an alkaline substance and was surprised to note improvement in the acetonemia and the asthma. It is suggested that the asthma in these patients may be due to a disturbance in the acid-base equilibrium in the sense of acidosis. Other patients have been reported as being benefited by acid therapy or a ketogenic diet.

ROSI, Chicago.

CONTRIBUTION TO THE STUDY OF THE MYCOSES; A CLINICAL CASE OF INFECTION WITH MYCOTORULA PINOYI AND RELATED EXPERIMENTAL STUDIES. V. SAGGESE, Riv. di clin. pediat. **32**:941 (Aug.) 1934.

A boy 6 years of age was brought to the pediatric clinic at Pisa for a chronic illness of two years' duration, characterized by vomiting, diarrhea, tenesmus and mild fever. He was poorly nourished and anemic (hemoglobin, 43 per cent); his color was yellow, and he had generalized adenopathy. A diagnosis of infection by Mycotorula (Monilia) pinoyi (cast) was finally made. Various treatments, including that with iodides, phenyl salicylate, methenamine, colonic irrigation and acetarsone, were of no benefit. The use of a vaccine prepared by the author produced favorable results, and six months later the child had recovered. Thirteen months later, although the child continued well, a few mycotorulae could still be cultured from the feces.

Experimental work with rabbits showed that the fundamental anatomic-pathologic lesion from the mycotorula infections is a mycotic granuloma.

HIGGINS, Boston.

DOLICHOCOLON. VIDAL JORDANA and TORRES MARTY, An. de pediat. **1**:271 (May) 1934.

In the past the subject of dolichocolon has been found mixed in with that of Hirschsprung's megacolon. The authors report two cases. In one case the diagnosis of chronic colitis had been made. The patient had had diarrhea several days a week, associated pain on the left side and at times nausea and vomiting. In the other case the diagnosis had been chronic appendicitis. The patient had pain localized to the hypogastrium and navel region, and he also had had attacks of diarrhea. Roentgen examination following barium sulfate enemas made possible the correct diagnosis. In chronic abdominal distress it is important to use the roentgen rays. It is not always easy to differentiate dolichocolon from megacolon. Dolichocolon is a disproportionate lengthening of one or various parts of the colon. The various etiologic theories are discussed. The treatment is surgical and medical. The authors treated both these patients medically by reducing the starches in the diet to a minimum and giving the patient a high protein diet. They believe that surgical treatment is too radical.

HERRON, Spokane, Wash.

ACUTE HEMOLYTIC ANEMIA. RAUL CIBILS AGUIRRE, CARLOS A. CORREAS and JUAN J. MURTAGH, Arch. argent. de pediat. **5**:330 (June) 1934.

The authors report this rather rare condition in a child aged 5 years. It developed in connection with a severe angina which proved to be diphtheria.

Certain infections and their resulting toxins produce both hemoglobinemia and hemoglobinuria. In certain cases of diphtheria, tetanus, scarlet fever, pneumonia, rheumatic fever and typhoid fever this symptom may develop. It is commonly observed in puerperal infection due to Bacillus perfringens and is occasionally seen in chronic paludism.

SCHLUTZ, Chicago.

ACCIDENTS ATTRIBUTED TO BLOOD TRANSFUSION. ANTONIO SELLEK Y AZZI, Arch. de med. inf. **3**:704 (June) 1934.

It is wrong to attribute to blood transfusion a series of accidents of which it is not the cause. When employing whole blood without adding citrate, the tests of homology being performed by an expert and the indication being correct, blood transfusion is the most harmless and at the same time the most heroic procedure which can be employed by the physician fearlessly in very different conditions.

SANFORD, Chicago.

BLUM'S PHENOMENA. P. A. SAINZ, Arch. de med. inf. **3**:747 (July-Sept.) 1934.

Sainz presents a case of Blum's phenomena (persistent vomiting or profuse diarrhea, resulting in acidosis, and elevation of the blood urea). He agrees with Chabanier that the syndrome is activated by a reduction of diuresis to relative oliguria. It usually starts in a previous nephritic process, but may be due to some occasional extrarenal pathologic condition. In the pure syndrome the pathology is hyperazotemia, chloropenia and alkalosis. Sainz also considers that it may include some protein dysmetabolism, with disintegration of tissues, with accompanying toxic phenomena. Sodium chloride therapy is specific. From 6 to 25 Gm. of sodium chloride should be given a day, subcutaneously, orally, intravenously or by rectum. Abundant liquids should also be given. The duration of the condition is from ten to thirty days.

SANFORD, Chicago.

MEGACOLON IN INFANCY. CALAZANS LUZ, Arch. de pediat., Rio de Janeiro **6**:871 (July) 1934.

Luz reviews the entire subject of megacolon in an excellent article of twenty-eight pages. The photomicrographs of sections of the large intestine are good.

SANFORD, Chicago.

CIRRHOSIS OF THE LIVER (LAËNNEC) IN A GIRL OF TEN YEARS. M. SORIANO-JIMÉNEZ, Paidoterapia **13**:27 (May) 1934.

Cirrhosis of the liver in childhood is uncommon. The girl when first seen had a large abdomen due to ascites. A collateral venous circulation was present in the enlarged abdominal veins. The Wassermann reaction was positive, also the Wassermann reaction of the father. The patient had often had sore throat and a cold. Six months ago swelling of the eyelids was noted; digestive upsets began two months ago, and then the abdomen was noticed to be increasing in size. Then edema of the legs appeared, which disappeared when the patient lay down. Five liters of clear ascitic fluid was removed. The child died a few days later. Autopsy confirmed the clinical diagnosis of cirrhosis of the liver. The yellow nodular liver weighed 570 Gm., and the firm spleen weighed 130 Gm. Sections removed for microscopic examination showed an increase in connective tissue and other changes common in sclerotic hepatitis.

The author believes that in this case the condition was due to alcoholism and syphilis combined. In few cases of this condition has the diagnosis been confirmed by autopsy.

HERRON, Spokane, Wash.

THE ALLERGIC CHILD: ACTUAL STATUS OF THIS QUESTION. M. PÉHU and P. WORINGER, Paidoterapia **13**:99 (June) 1934.

Only the noninfectious causes of allergic conditions are discussed. Infantile allergy may be congenital or acquired. Of the various hypotheses the authors favor that which maintains that congenital allergy is a hereditary property of the organism that is transmitted by the germ cells. They do not have much confidence in the theory that allergic sensitivity takes place in utero by the transmission through the fetal circulation of the toxins that produce the allergic phenomena. Many of their patients show the same allergic sensitivities that their parents do and are sensitive to substances with which they have never come in contact. The superficial skin tests are more convenient but are less reliable and less sensitive than the intradermal skin tests. Bloch of Zurich devised a skin test in which the material to be tested is laid directly on the skin and covered with a piece of gutta percha, no scratch being made. The reaction is read in twenty-four hours. This is the same as the patch test in this country.

Clinical cutaneous manifestations of allergy are urticaria, various exanthems, purpura and infantile eczema. Respiratory manifestations are conjunctivitis, rhinitis and pollinosis, produced by pollens and vegetable substances. Digestive hypersensitivity may be congenital or acquired. The congenital type shows up in the first few days of life; the acquired is present from the second week of life and is the more common. Other types of allergy include anaphylaxis, epilepsy and migraine. In all cases the type of allergy is distinct for each person. The authors do not believe that allergy is more frequent in infants than in adults.

HERRON, Spokane, Wash.

CHRONIC SUBMAXILLARY ADENITIS OF DENTAL ORIGIN. J. MAYORAL, Paidoterapia **13**:345 (Aug.) 1934.

Much chronic submaxillary adenitis that is thought to be tuberculous is of dental origin and disappears on extraction of decayed teeth. In many cases the tuberculous process follows infection of these glands. The doorway of infected teeth is recognized as the entrance way of the tubercle bacillus, which follows the capillary lymphatics of the teeth. All children with cervical adenitis are sent to the dentist for care of decayed teeth. Examination of the teeth should be made twice a year by a dentist to prevent acute and chronic submaxillary adenitis and the subsequent tuberculous infection of these glands. HERRON, Spokane, Wash.

DWARFISM IN PEDIATRICS. OLAVO LUSTOSA, Pediatria, Rio de Janeiro **1**:189 (June) 1934.

The author illustrates by photographs, roentgenograms and case histories cases of rickets, chondrodystrophy, hypothyroidism, infantilism and mongolian idiocy.

SANFORD, Chicago.

SUBCUTANEOUS GENERALIZED EMPHYSEMA FOLLOWING BRONCHOPNEUMONIA AND SCARLET FEVER. CARLOS F. DE ABREU, Pediatria, Rio de Janeiro **1**:212 (June) 1934.

De Abreu reports the case of a boy, 21 months old, and photographs are shown of the emphysema, which was generalized. The child died of the condition. The author has no explanation to offer for the predisposition to this condition.

SANFORD, Chicago.

SUBPHRENIC ABSCESS IN EARLY INFANCY. ADAUTO DE REZENDE, Pediatria, Rio de Janeiro **1**:285 (Sept.) 1934.

A 14 month old boy had a digestive disturbance for six days. On the last days of the illness there was some cyanosis, and a few râles were heard at the

base of the lower lobe of the right lung. These had disappeared on the twelfth day, and the temperature was normal. On the sixteenth day the temperature rose and the liver was distinctly large. There was also leukocytosis. Four days later there was a diminution to percussion in Traube's space, and the diagnosis of subphrenic abscess was made. This was confirmed by roentgenograms. The operation was successful, and the boy made an uneventful recovery. Staphylococcus was cultured from the abscess.

SANFORD, Chicago.

TEMPERATURE VARIATIONS. JAIME FREIRE DE VASCONCELOS, Pediatria, Rio de Janeiro **1**:292 (Sept.) 1934.

The author made studies of the variations in the oral, axillary and rectal temperatures in one hundred children of various ages. There was a great difference in the individual variations, which are shown nicely in the author's charts. On the average, the oral temperature varied from 0.2 to 1.2 (3.6 to 1.92 F.) above the axillary temperature, and the rectal temperature varied from 0.1 to 0.8 C. (0.18 to 1.44 F.) above the oral temperature. The general average was a rectal temperature 0.5 C. (0.9 F.) above the oral temperature, with an axillary temperature 0.8 C. below the oral temperature.

SANFORD, Chicago.

PINWORMS AND OXYURIASIS. FRANZ HAMBURGER, Arch. f. Kinderh. **102**:223 (July 31) 1934.

A few pinworms in a child's stool should be no cause for worry, as they do not affect the health, occur frequently and are of no significance. They do not require energetic treatment. Hamburger believes that the physician should be careful not to alarm the mother when an occasional pinworm is accidentally found. However, when there are hundreds or thousands of pinworms present the condition is true oxyuriasis, and the worms should be eradicated. Garlic infusion enemas and santonin given by mouth are recommended. In most instances picking the nose and scratching the anus are habits and not due to infestation with pinworms.

LEMASTER, Evanston, Ill.

FAMILIAL LYMPHOCYTOSIS. H. RICHTER, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **138**:172 (Aug. 22) 1934.

Richter presents two patients, aged 13 and 21, respectively, showing a constant lymphocytosis with a normal or slightly subnormal total number of leukocytes. The first indication for an examination of the blood in each case was an acute inflammatory pharyngitis accompanied by swelling of many lymph nodes. The first case was one of acute pharyngitis; the second, one of gangrenous angina. In both cases the lymphocytosis was still demonstrable after complete recovery. In close relatives of the patients the general state of the blood was characterized by lymphocytosis. Richter concludes that the tendency to lymphocytosis is familial and hence constitutional. He attributes a secondary rôle to the infection.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

TUBERCLE BACILLI IN THE BLOOD AND SPINAL FLUID IN CHOREA. E. LOEWENSTEIN, Med. Klin. **30**:1300 (Sept. 28) 1934.

In patients with chorea Dr. Loewenstein found tubercle bacilli not only in the blood stream but also in the spinal fluid. Centrifugated sediments of spinal fluid showed organisms in smears stained by the Ziehl-Neelsen method, by animal inoculations and in cultures. Cultures were positive for tubercle bacilli in six of the seven cases of chorea studied.

DOOLEY, New York.

A Large Bladder Stone in a Child. G. Freund, Med. Klin. **30**:1334 (Oct. 5) 1934.

This is the autopsy report of a 20 month old boy who died of scarlet fever complicated by bronchopneumonia. A stone composed of calcium phosphate and uric acid and measuring 4.5 by 2.5 cm. was found in the bladder. There were dilatation, hypertrophy and chronic inflammation of the left ureter and hydronephrosis on the left. During life the child had no symptoms referable to the urinary tract.

Dooley, New York.

The Venous Pulse in Children. W. Ochse and E. Püschel, Monatschr. f. Kinderh. **60**:401, 1934.

The authors describe a technic for taking the venous pulse rate in children. A hair wire is enclosed in a container placed over the vein and the vibrations transmitted to a drum with photosensitive paper. A tracing is included. In children the A wave is generally low and in terms of millimeters, smaller than the C wave. The ascending arm of the former is more gradual than the latter. The duration of the A wave was three thirtieths of a second, but this may not be absolutely accurate, as often the beginning is not well delineated. The systolic drop following C is designated as X and is about the same as in adults. In relation to the second heart tone, the deepest point of the systolic drop occurred from one-hundredth to two-hundredths second previously and immediately before the diastolic rise. D and Y are about the same as in adults.

Gerstley, Chicago.

The Pneumococcus Problem in Childhood. Gerhardt Joppich, Monatschr. f. Kinderh. **60**:407, 1934.

Joppich reports cases, with temperature curves, roentgen findings and observations at autopsy, showing the variability of pneumococcic manifestations in infancy. Many times the roentgen rays did not give an accurate picture of what was occurring. The author used this material to try to throw some light on why some types of pneumonia are lobular and some globular. Some investigators believe the difference to be due to the different types of pneumococci; others think that they depend on differences in the reaction of the human organism. In his material the author collected several instances in which on autopsy both types of pneumonia were present. Bacteriologically, all areas showed pneumococci of the X type. Studies of antibodies and virulence were of little help. He concludes that the problem cannot be solved as yet.

Gerstley, Chicago.

Auto-Injection of Urine. Martin Krebs, Monatschr. f. Kinderh. **60**:442, 1934.

With little scientific explanation Krebs states that he tried the effect of autoinjections of urine on children suffering from anaphylactic manifestations. To 5 cc. of urine he added 1 drop of phenol. The initial dose is from 0.2 to 0.5 cc. given intramuscularly every three to four days. He claims that following the inoculation there was relief from hay fever, asthma, serum sickness, eczema and conditions associated with spasms, such as whooping cough and spastic conditions following injury at birth.

Gerstley, Chicago.

Generalized Xanthomatosis. K. Herman, München. med. Wchnschr. **81**:1100 (July 20) 1934.

The symptomatology of generalized xanthomatosis was first described by Hand in 1893. In 1928 Rowland showed that the fundamental disturbance was in the cholesterol metabolism. The cholesterol may be deposited in various parts of the body but is found most frequently in the hypophysis, tuber cinereum, dura mater, bones of the skull, tonsils, skin, lungs, liver, spleen and lymph nodes. The symptoms vary, depending on the tissues or organs involved. As a result of the presence

of cholesterol a specific granulation tissue is formed, and for that reason the disease complex has also been called lipoid granulomatosis. Deposits of keratin produce Niemann-Pick's disease; deposits of phosphatides produce Gaucher's disease, and deposits of cholesterol produce xanthomatosis. Herman reports a typical case of generalized xanthomatosis.

BRAHDY, Mount Vernon, N. Y.

A COPROLITH CONTAINING BISMUTH AS A COMPLICATION OF HIRSCHSPRUNG'S DISEASE. A. Kovács, Röntgenpraxis **6**:164 (March) 1934.

On examination of a patient with megacolon a coprolith became visible in the lower part of the pelvis, taking the form of a large tumor formed in concentric layers. It weighed 740 Gm. and was found to consist largely of bismuth from successive roentgen examinations.

VINTON, Brooklyn.

ACUTE CARDIAC PULMONARY EDEMA AND ITS REFLEX MECHANISM. S. WASSERMANN, Wien. Arch. f. inn. Med. **24**:387 (Feb.) 1934.

Acute cardiac pulmonary edema in certain clinical cases represents a reflex syndrome of the cardiopulmonary vegetative nervous system. It can be improved or entirely suppressed by pressure on the carotids.

Pulmonary edema usually occurs spontaneously and is accompanied by an increased heart rate, a rise in the blood pressure and stimulation of the sympathetic nerve. The attack is accompanied by a series of subjective and objective symptoms. Among the subjective symptoms can be mentioned feelings of oppression, strangulation and asphyxiation. Among the objective symptoms can be mentioned an agonizing dyspnea, moist râles of both lungs and serohemorrhagic sputum. The effect of pressure on the carotids represents a complex and antireflex which produces vasodilatation.

The point of the development of the pulmonary edema reflex lies in the coronary-aortic innervation. It involves primarily the sympathetic paths, among them the stellate ganglions, the rami communicantes, certain regions in the spinal cord and medulla, the spinal and subcortical centers and, finally, the cortex. Clinical conditions which favor its development are aortic and coronary sclerosis, infarction of the left ventricle, mesaortica luetica, endocardial aortic insufficiency and hypertonicity of the heart muscle.

Spontaneous attacks of pulmonary edema are not confined to the night period but may occur at any time. Angina pectoris and cardiac asthma may simulate closely attacks of pulmonary edema.

In the treatment of the attacks the effect of pressure on the carotids should be attempted. Sedation of the central breathing mechanism through opiates is valuable. Hot foot baths and a sinapism applied to the precordium and over the back produce favorable reflex influences. Alcohol, amyl nitrite and nitroglycerin are remedies which produce a favorable effect in relieving spasmodic manifestations. Supporting measures are inhalations of oxygen, moderate blood-letting, the use of digitalis and other cardiac stimulants. During the intervals of the attacks sedative remedies may be used which reduce irritability and reflex susceptibility. Among these chloral hydrate, bromides, codeine and barbituric acid compounds are of value. For sedation of the neurovascular heart-lung apparatus quinine, papaverine or theobromine may be used. A dry diet, restriction of fluids and moderate use of diuretics is indicated. The intermittent use of digitalis is sometimes of value.

SCHLUTZ, Chicago.

RESULTS OF SPLENECTOMY IN GAUCHER'S DISEASE. O. ULLRICH, Ztschr. f. Kinderh. **55**:1 (May) 1933.

Ullrich reports a case of Gaucher's disease in a 33 month old boy on whom a splenectomy was performed. The severe anemia and the hemorrhages subsided a short while after the splenectomy. On the other hand, osseous changes were noticed roentgenologically after the operation. Ullrich comes to the conclusion

that splenectomy should be performed in Gaucher's disease only when life is threatened through anemia and hemorrhages. Otherwise it should not be done.

LEVINSON, Chicago.

RETICULO-ENDOTHELIOSIS—A NEW MANIFESTATION IN THE HEPATOSPLENOMEGALIES. STURE A. SIWE, Ztschr. f. Kinderh. **55**:212 (July) 1933.

Siwe reports several cases of hepatosplenomegalies in childhood with reticulo-endothelial hyperplasia with the following characteristics: marked splenic enlargement; moderate or marked enlargement of the liver; moderate or marked swelling of the internal and external lymph nodes; marked tendency to bleeding, particularly in the form of purpura; moderate secondary anemia; no leukocytosis or leukopenia; no monocytosis, a normal or increased number of thrombocytes; an acute onset with fever, with or without demonstrable infection; a rapid downward course resulting in death, the disease lasting several weeks to several months; negative blood cultures; marked reticulo-endothelial hyperplasia seen on splenic puncture, with leukocytes but without any eosinophilia and without typical cell inclusion such as occurs in Gaucher's disease and Niemann-Pick's disease.

The etiology cannot as yet be definitely stated. Most likely the disease is of infectious origin, but it is hard to say whether infection directly causes the hyperplasia or whether the latter is a result of a metabolic disturbance of unknown nature.

LEVINSON, Chicago.

NEUROGENIC AND CONSTITUTIONAL COMPONENTS IN THE ORIGIN OF THE PROTRACTED SUBFEBRILE TEMPERATURE. Y. Y. SHPIRT, Vrach. delo **17**:187, 1934.

The author has studied clinically 220 patients with protracted subfebrile elevations of body temperature. Only 124 of them presented difficulties as to the diagnosis and the solution of the question of their capacity for work. After exclusion of infectious and thyrogenic disorders there remains a group of neurogenic and constitutional conditions, which form the subject of the present study. Elaborate clinical and laboratory investigations of the patients did not reveal any noticeable pathologic changes but for the temperature alone, which showed permanent subfebrile elevations, the temperature pattern being of a monotonous character without great daily oscillations and showing typical reactions to strychnine and morphine, with marked tachycardia and superficial type of heart contractions on roentgen examination. The patients had been under observation for one and one-half years but showed no changes of the clinical picture. Few complained of heart disturbances. The rest had no complaints and thought themselves in good health. Almost all the patients are asthenic and have had influenza or tonsillitis. The instability of the thermoregulating center in asthenia, which is liable to be upset in consequence of slight infections, may be the cause of the disease in question.

YAMPOLSKY, Atlanta, Ga.

A CASE OF SCHÜLLER-CHRISTIAN DISEASE. G. TSUCHIYA and T. KAKU, Acta soc. ophth. jap. **38**:116 (Aug.) 1934.

This is the second case of Schüller-Christian disease which has been reported by ophthalmologists in Japan. A boy 4 years of age who, until the development of his present trouble, had been well from the time of birth, now presents a left exophthalmos, which has been progressive for one year. There is a large defect in the bones on the left side of the skull. The eyes otherwise are perfectly normal.

KNAPP, New York. [ARCH. OPHTH.]

A NEW METHOD FOR OBTAINING TISSUE FLUID IN CHILDREN. L. O. FINKELSTEIN, F. S. MERSON and E. E. GOLKWER, Acta pædiat. **15**:330 (June 5) 1934.

There are numerous reasons why a more thorough knowledge of the chemical composition of tissue fluid is necessary to augment the understanding of cellular

physiology. Tissue fluid, however, is difficult to obtain. Material collected at autopsy is an entirely unsatisfactory substitute for the interstitial fluid of living subjects; the same is true of inflammatory exudates and transudates. The analysis of excreta does not supply the desired information.

Since the skin is so immediately accessible during life, several methods have been devised whereby it can be made to yield intercellular fluid. Most of these procedures involve an excessive amount of trauma. Urbach, for example, employs a punch biopsy by means of which he obtains a circular portion of skin weighing from 120 to 160 mg. The fluid is extracted from this material in a Buchner hydraulic press. Despite the claims of the proponents of the method, the liquor so obtained cannot be regarded as unmixed interstitial fluid. Gännslen produces a vesicle on the skin by applying a cantharidin plaster. He asserts that the content of the vesicle is "only slightly altered tissue fluid." Because of the inflammatory character of the bulla this claim cannot be accepted at its face value.

The authors present a technic for producing a cutaneous vesicle which does not involve trauma or inflammatory reaction. In simplest form their method consists simply in cupping a suitable surface of the skin until a blister forms. It is somewhat more satisfactory to use a modified cupping-glass which can be evacuated with a mechanical pump under manometric control. The time required for the appearance of the bleb depends on the area chosen, as well as on the age and the state of health of the subject. In general, this technic gives more rapid results than other methods.

The physiologic mechanism behind the production of the bulla consists essentially in the alteration of the relationships normally existing between intravascular and extravascular pressure in such a manner that fluid flows from the capillaries into the tissue. Consequently one would expect the contents of such bullae to have the chemical characteristics of edema fluid. The authors confirmed this expectation by chemical analyses, the results of which are reported. For comparison they include data concerning the composition of the fluid of blisters simultaneously produced by cantharidin and of blood serum obtained at the same time.

McCune, New York.

Nonrachitic Soft Chest. Nicolai Johannsen, Acta pædiat. **15**:374 (June 5) 1934.

Although craniotabes was formerly regarded as a phenomenon due exclusively to rickets, it is now recognized that softening of the skull may occur in healthy infants who show neither chemical nor roentgenologic evidence of rickets. The same statement may be made with regard to softening of the bones of the chest. Appleton observed numerous examples of soft thorax among Japanese and Chinese children in Hawaii, where rickets is rare. Hess reported similar cases in which softening of the chest was associated with flattening of the occiput, cranial asymmetry and flatfoot. In his patients the absence of systemic rickets was confirmed by chemical and roentgenologic examination and, in two instances, by autopsy. Hess regards the condition as one of congenital or developmental osteoporosis bearing no relationship to rickets. It is important to note that the deformity of the chest in these patients is not identical with that known as Harrison's groove. On the contrary, it is limited to the anterior part of the thorax and to the lower end of the sternum and the surrounding costal wall. It results chiefly in permanent deformities of the type known as flat chest, funnel chest or pigeon chest.

Five cases of soft chest in infants and children are reported. In all these the presence of rickets could be excluded with reasonable assurance.

McCune, New York.

Bilateral Spontaneous Pneumothorax. Torben Geill, Hospitalstid. **77**:587 (May 15) 1934.

The author reports a case of bilateral pneumothorax in a 14 year old boy suffering from bronchial asthma and emphysema of the lungs. The condition had

developed slowly in sequence to a severe attack of asthma more than a year before, first on the left side and subsequently on the right. When seen the patient was in a dangerous condition with pronounced cyanosis and dyspnea, but he improved on aspiration of air from the left lung. In two months the pneumothorax became completely absorbed, and on reexamination about nine months later no remaining trace of the condition could be discovered.

VINTON, Brooklyn.

A CASE OF HERTER'S DISEASE WITH CHRONIC PULMONARY INFECTION. G. J. HUET, Maandschr. v. kindergeneesk. **3**:343 (June) 1934.

Huet reports a case of this condition, with the results of necropsy, and gives a survey of cases of Herter's disease in which the pancreas was especially affected.

VAN CREVELD, Amsterdam, Netherlands.

SPORADIC HEMORRHAGIC DIATHESES. S. VAN CREVELD, Maandschr. v. kindergeneesk. **3**:351 (June) 1934.

A case of acute hemorrhagic edema and one of sporadic hemophilia are described. The clinical picture and the changes in the blood in the last-mentioned case are minutely reported and compared with those in a patient who had hemophilia (hereditary), studied at the same time. The question of the cause of the hemophilia is further discussed in consequence of some research on both the children with hemophilia. The attention is especially drawn to a factor favoring coagulation, which is present in normal serum and in euglobulin, but which is probably absent in the serum of hemophilic persons. There is a discussion of the therapy of hemophilia.

AUTHOR'S SUMMARY.

CALCINOSIS INTERSTITIALIS PROGRESSIVA. H. A. VAN DER STERREN, Maandschr. v. kindergeneesk. **3**:396 (July) 1934.

A typical case of this rare disease in a girl of 5 years is described. In the literature there is great confusion as to the etiology, pathology, disturbance of the metabolism, histologic changes and therapy, as the different disorders of this type are not sufficiently distinguished from each other. The author gives a practical scheme for the classification of the different diseases in which formations of calcium and bone are found.

VAN CREVELD, Amsterdam, Netherlands.

ETIOLOGY OF RHEUMATISM IN CHILDHOOD. J. VAN LOOKEREN CAMPAGNE, Maandschr. v. kindergeneesk. **3**:418 (July) 1934.

The author gives a survey of the progress of the study of the etiology and pathogenesis of rheumatism in childhood and discusses the recent pediatric literature, especially American and English on polyarthritis rheumatica acuta and cognate diseases. Special stress is laid on the allergic theory.

VAN CREVELD, Amsterdam, Netherlands.

THE ROUTE OF INFECTION IN WEIL'S DISEASE. P. H. VAN THIEL, Nederl. tijdschr. v. geneesk. **78**:3115 (July 7) 1934.

Unanimity exists about the capacity of Leptospira icterohaemorrhagiae to invade the human organism by the skin, especially when the latter is damaged, as well as by the mucous membranes, even of the upper digestive tract, but it is not known as yet by which route this disease, which some years ago was rather frequent in Holland, occurs most often and most easily. The problem has shown a new aspect by the Weil epidemic at Lissabon, caused by infected water. For a better insight into this problem investigations were done with rats and guinea-pigs, which proved that although the possibility of oral infection exists, several millions of spirochetes may be swallowed by the animals without causing the disease. The infection is

brought about much more easily by the nasal route and also by way of the conjunctiva. Water snuffed up the nose is probably more dangerous for swimmers than swallowed water.

VAN CREVELD, Amsterdam, Netherlands.

AGRANULOCYTOSIS (MALIGN NEUTROPENIA) CAUSED BY DRUGS. J. GROEN and C. J. GELDERMAN, Nederl. tijdschr. v. geneesk. **78**:3444 (July 28) 1934.

Thirteen cases of agranulocytosis, observed in the Wilhelmina-Gasthuis at Amsterdam, were investigated in order to detect whether any relation existed between the drugs that the patients had used and the disease. In two patients neoarsphenamine was a causative agent; nine patients had been taking some drug containing antipyrine or aminopyrine, often in combination with some other compound, before the onset of their symptoms. Usually the drug was used in the treatment of some painful or febrile condition. In one case increase in the number of leukocytes and recovery from the necrotic angina were observed after discontinuation of the aminopyrine medication. In two cases an inquiry among the physicians who had been treating the patients before their admission revealed the use of only acetylsalicylic acid, sodium salicylate and quinine sulfate, but the possibility that other drugs had been taken could not be excluded. Five additional cases are described which had been observed elsewhere; in every case some compound containing aminopyrine had been used.

The significance of these observations is discussed, and the following conclusions are reached: An outbreak of agranulocytosis may follow the use of various drugs. Among these, antipyrine and aminopyrine have a definite etiologic significance. The possibility of a similar effect of other antipyretics and hypnotics (especially of the barbiturates) must be borne in mind. The danger of the occurrence of an agranulocytotic syndrome following the administration of drugs is probably restricted to certain allergic persons. Many of the present conceptions about agranulocytosis must be revised; a toxic etiology of agranulocytosis appears to be the rule rather than the exception. During the administration of antipyrine or aminopyrine a continuous supervision of the leukocyte count is imperative.

VAN CREVELD, Amsterdam, Netherlands.

A CASE OF LIPODYSTROPHIA PROGRESSIVA. P. H. VERSPYCK, Nederl. tijdschr. v. geneesk. **78**:3792 (Aug. 18) 1934.

A boy of 12 years with lipodystrophia progressiva is described. The author compares this disease with regional adipositis.

VAN CREVELD, Amsterdam, Netherlands.

Nervous Diseases

THE NEUROLOGIC ASPECT OF VOLUNTARY, AUTOMATIC AFFECTIVE AND SPONTANEOUS PHENOMENA IN THE INFANT, CHILD AND ADULT. SAMUEL WEINGROW, Arch. Pediat. **51**:624 (Oct.) 1934.

This article cannot be satisfactorily abstracted.

WADDELL JR., University, Va.

CONVULSIONS IN CHILDHOOD. M. G. PETERMAN, J. A. M. A. **102**:1729 (May 26) 1934.

Peterman presents a revision of his former classification of convulsions in childhood based on the study of five hundred cases. In 33 per cent the basic diagnosis was epilepsy; in 22.8 per cent the convulsions occurred at the onset of an acute infection, and in 15.4 per cent cerebral injury at birth or residue was responsible. Spasmophilia accounted for 13.6 per cent and miscellaneous causes for 8.8 per cent. In 6.4 per cent the cause was unknown. Six and six-tenths per

cent of the convulsions appeared in the first month of life, 13.6 per cent in the second to the fifth month, 40.2 per cent between the sixth and the thirty-sixth month; 26.4 per cent between 3 and 10 years of age and 6.4 per cent between 10 and 15 years. The author was unable to recognize the presence of allergic conditions which might have been responsible for the convulsions, nor was he able to find in his series any convulsions that could be attributed to hypoglycemia, hyperinsulinism or cerebral sinus thrombosis.

BONAR, Salt Lake City.

STREPTOCOCCUS (VIRIDANS) MENINGITIS WITH RECOVERY. J. FELSEN and A. G. OSOFSKY, J. A. M. A. **102**:2170 (June 30) 1934.

Fifty-seven cases of recovery from streptococcic meningitis have been reported. Streptococcus viridans was involved in only four of these. In the case reported injection of gas gangrene serum was followed by such a prompt change for the better that immunologic studies were made. The gas gangrene serum increased the degree of phagocytosis of rabbit cells on blood agar plates. While the possible value of the injection of gas gangrene serum in this case is pointed out. Felsen and Osofsky do not believe that it can be advocated as a specific, for other serums might have acted similarly or spontaneous recovery might have occurred anyway.

BONAR, Salt Lake City.

FAMILIAL PERIODIC PARALYSIS AND ITS TRANSITION INTO SPINAL MUSCULAR ATROPHY. A. BIEMOND and A. POLAK DANIELS, Brain **57**:91 (June) 1934.

A description of the first Dutch family in which periodic paralysis appeared in three generations (fourteen cases) is given. In one of the cases chemical analyses were performed during an attack and during an interval; the results point to a shift in the sympathicotonic direction. The pathophysiology is suggestive of an important alteration of the chemistry of some of the striated muscles. Anatomic examination offers no help concerning the essential nature of the disease. There is a distinct type of spinal muscular atrophy which occurs in connection with familial periodic paralysis. By adopting the presence of two pathologic hereditary factors, both being dominant, the authors believe they have found a genetic explanation, according to Mendel's law, for this family.

MICHAELS, Boston. [ARCH. NEUROL. & PSYCHIAT.]

THE MYOTONIA ACQUISITA IN RELATION TO THE POSTNEURITIC MUSCULAR HYPERTROPHIES. KNUD H. CRABBE, Brain **57**:184 (June) 1934.

Crabbe describes three cases in which true muscular hypertrophy (different from the pseudohypertrophy of the progressive myopathies) developed after an acute illness. In one case the hypertrophy was associated with myotonic symptoms; in the other two no myotonia was observed. If the muscle hypertrophies as a whole, no myotonia results; if the sarcoplasm especially hypertrophies a myotonic condition will be the consequence. In the thirty-four cases of myotonia acquisita reported in the literature all the patients were male and the age of onset (when given) was between 15 and 45 years. It is concluded that myotonia acquisita and true muscular hypertrophy are variations of the same abnormality: an abnormal regeneration after a neuritic process.

MICHAELS, Boston. [ARCH. NEUROL. & PSYCHIAT.]

THE PARTICIPATION OF THE NEUROGLIA IN THE FORMATION OF MYELIN IN THE PRENATAL INFANTILE BRAIN. BERNARD J. ALPERS and WEBB HAYMAKER, Brain **57**:195 (June) 1934.

From a study of the literature Alpers and Haymaker believe that there is good evidence that oligodendroglia cells and deposits of myelin are intimately related. Brains of premature infants ranging in age from 5 to 9 months were

studied by means of specific stains for neuroglia. That the astrocytes probably play a part in the function of deposit of myelin about the axis-cylinder is shown by the presence of fat in the astrocytes during myelinization.

MICHAELS, Boston. [ARCH. NEUROL. & PSYCHIAT.]

CASES OF MEDIAN NERVE PALSY PRODUCED BY ATTEMPTED INTRAVENOUS INJECTIONS OF CALCIUM CHLORIDE. HARLEY STEVENS, Brit. J. Child. Dis. **31**:117 (April-June) 1934.

The first case was that of a girl, 13½ years of age, who was admitted to the hospital for tuberculous peritonitis. To relieve abdominal pain of a colicky nature she was given intravenous injections of 5 cc. of a 10 per cent solution of calcium chloride. In the course of one of these injections she complained of tingling and pain in the thumb and palm of the left hand (the left median basilic vein was used). The following day there were complete motor palsy of the median nerve and also anesthesia of the region supplied by the lateral palmar branch. These signs persisted until the patient died three months later.

Two similar occurrences in adults are added, and Zutt's five cases are also cited.

The reader is reminded that the median cutaneous nerve of the forearm lies immediately adjacent to the median basilic vein on its medial aspect and in the same tissue plane. The median nerve lies behind the vein and is separated from it by the dense deep fascia.

LANGMANN, New York.

THE MEDICINAL TREATMENT OF CHOREA. N. MUTCH, Brit. M. J. **2**:246 (Aug. 11) 1934.

Chorea is classified in this article more or less conventionally as mild, moderate and severe. Mutch reviews briefly the various treatments, the drugs used and the method of administration. A brief discussion concerning the favorable and unfavorable results of treatment by phenyl-ethyl-hydantoin, by the ketogenic diet and by pyrogenetic methods follows. Three etiologic factors in the production of chorea—rheumatism, nervous strain and calcium deficiency—are then discussed. The author dwells particularly on the last, calcium deficiency. He quotes Warner and his theories to the effect that in active chorea there is always calcium deficiency, which is greater in severe than in mild cases. He emphasizes that a disturbance in calcium metabolism occurs, but its causation is still a matter for research.

Then follows a discussion of calcium acetylsalicylic acid, which the author thinks replenishes the means of healing with the three etiologic factors simultaneously. The drug, dissolved in water, is administered by mouth, the average daily dose varying up to 45 grains (2.9 Gm.) for a child of 12 years. The author thinks that not only satisfactory but often dramatic results are obtained by the administration of this drug. He claims first that it occasions no exhaustion, discomfort or risk to the patient. It is less toxic than acetylsalicylic acid and is free from the irritant action of the parent substance on the stomach and bladder. It is soluble, tasteless and rapidly absorbed. It is (1) antirheumatic, (2) corrective of calcium deficiency and (3) a sedative to the brain.

ROYSTER, University, Va.

THE PROBLEM OF STUTTERING: THE PRESENT POSITION. GEORGE SETH, Edinburgh M. J. **41**:497 (Aug.) 1934.

This communication comes from the University Psychological Clinic for Children and Juveniles in Edinburgh.

World-wide investigations indicate that about 1 per cent of the school population stutters. Stuttering occurs more frequently among mentally retarded than among normal children. The sex incidence is four or five boys to one girl. Racial difference in incidence is illustrated by the fact that in the nationalities with a high cephalic index, as the "broad-heads" of Poland and Russia, stuttering is common. It is less common in Southern Europe among the "narrow-heads."

Stuttering is notably a disturbance of childhood and appears gradually, several years elapsing before the child is taken for examination or treatment. Most stuttering begins before school age, and in Edinburgh it begins under the age of 8 years in 93 per cent of the cases.

The first problem or danger point is found not at the beginning of speech but at the time of change from echolalia (echo speech) to the voluntary control of speech as a social function of the individual. Seth's cases show that nearly one half of those affected begin to stutter at the age of four or five years. The new environment of school life makes a sudden demand on the powers of expression at an immature period of life.

Stuttering is due not to difficulty in pronouncing speech sounds but in making the transition from one syllable or word to the next, a disintegration of coordinated function. The defect is in the subject's "breath control" and not in his respiration. He does not breathe rhythmically when required, even when not attempting to speak.

In 30 per cent of the cases at the psychologic clinic there existed evidence of chronic anxiety. Seth discusses the various interpretations of the disorder, namely physiologic, psychologic and psychoanalytic. He states that in a not inconsiderable number of his cases there was a prevalence in childhood of nutritional neurotic manifestation of thumb-sucking and nail-biting and difficulties in feeding. In the child who is beginning to stutter the excessive contractions of the oral musculature of older stutterers is absent.

NEFF, Kansas City, Mo.

THE CHLORIDES IN MENINGITIS. L. O. FINKELSTEIN AND F. S. MARSON, Rev. franç. de pédiat. **10**:204, 1934.

The chlorides of the cerebrospinal fluid, of the blood and of the tissue fluid were determined in forty-one cases—twenty-three of cerebrospinal meningitis, nine of tuberculous meningitis, one of purulent meningitis, four of aseptic serous meningitis and one of syphilitic meningitis and in three normal persons. In normal children and in those with aseptic and syphilitic meningitis the chlorides of the cerebrospinal fluid and of the tissue fluid were well above those of the blood. In tuberculous meningitis the chlorides of the tissue fluid and of the cerebrospinal fluid approached those of the blood. In meningococcus meningitis the lowering of the chlorides of the cerebrospinal fluid and of the tissue fluid, although not usually as great as in tuberculous meningitis, parallels the severity of the infection, and their determination is valuable from the point of view of prognosis. The authors conclude that the lowering of chlorides in the cerebrospinal fluid indicates a demineralization of the organism, and this should be taken in consideration in the dietary regimen.

LESLIE, Evanston, Ill.

LATE AMAUROTIC IDIOCY OF THE VOGT-SPIELMEYER TYPE, WITH RETINITIS PIGMENTOSA: RELATIONS TO NIEMANN-PICK'S DISEASE. G. MARINESCO, Rev. d'oto-neuro-opht. **12**:39 (Jan.) 1934.

The problem of the intimate relationship of amaurotic idiocy with Tay-Sachs' and with Niemann-Pick's disease involves also the late forms in which the lesions affect the central nervous system, the parenchyma of other organs and the reticuloendothelial apparatus. There is difference of opinion as to this relationship, but Kufs thought that one is not justified in denying it because the two diseases do not always coincide. He also believed that involvement of the central nervous system depends less on the neuro-ectodermal origin than on the histochemical structure of its elements. Junius believed that there is a relationship between familial amaurotic idiocy, Niemann-Pick's disease and Gaucher's disease. In the case of Gaucher's disease reported by Lindau and Lund the histologic lesions of the neuraxis resembled those of amaurotic idiocy, and even the eyeground showed changes like those in Tay-Sachs' disease.

The case of a girl, aged 9 years, in which an autopsy was performed, is reported. The report of the autopsy is confined to a description of the retinal changes, which included especially profound alterations in the layer of rods and cones, disappearance of the internal granular layer and fatty degeneration of the nerve cells.

DENNIS, San Diego, Calif. [ARCH. NEUROL. & PSYCHIAT.]

EPILEPSY, TETANY AND CATARACT. H. ROGER, Y. POURSINES and M. RECORDIER, Rev. d'oto-neuro-opht. **12**:43 (Jan.) 1934.

The case is presented of a patient, aged 22, who had had epilepsy since infancy. At the age of 15 tetany appeared, and five years later an evolutive endocrine cataract was observed (the calcium content of the blood was reduced to 0.0082 Gm. per liter). Slight and variable passive hypertonia and intentional contracture of the lower limb, general muscular asthenia, nightmares and somnambulism were also present. The association of tetany and epilepsy and that of tetany, spasmophilia and epilepsy have been reported in the literature. In the case reported here the epilepsy was traced to an encephalopathy, of unknown nature, occurring in infancy, as was also the dystonic subcortical syndrome; a syphilitic origin seems probable. A number of cases of an association of cataract with tetany have been reported. According to Peters, there is a lesion of the ciliary epithelium which produces a molecular concentration of the liquid of the anterior chamber and an alteration of the crystalline medium.

DENNIS, San Diego, Calif. [ARCH. NEUROL. & PSYCHIAT.]

COMBINED MENINGOCOCCIC AND TUBERCULOUS MENINGITIS. G. CARLONI, Clin. pediat. **16**:610 (July) 1934.

Carloni reports two fatal cases of meningitis in which both tubercle bacilli and meningococci were present in the meninges at autopsy. One patient was 1 year old; the other, 6 months of age. The author also reviews the literature with reference to this unusual combination of diseases.

DOOLEY, New York.

ENCEPHALITIS IN CHILDREN: I. EPIDEMIC ENCEPHALITIS. A. FIANO, Riv. di clin. pediat. **32**:513 (May) 1934.

Fiano reports ten cases of epidemic encephalitis seen in the pediatric clinic in Florence. Several patients were seen with the acute stage only and several with the stage of sequelae, and three have been followed for about ten years during both stages.

HIGGINS, Boston.

MYELOMUSCULAR DYSPLASIA. A. GENTILI, Riv. di clin. pediat. **32**:835 (July) 1934.

Gentili reports the cases of two children with primary myopathy. In the first patient, a baby of 5½ months, muscular weakness was first noted two months previously and had gradually progressed. After considering the possibility of Oppenheim's disease and the Werdnig-Hoffmann type of muscular atrophy, the author finally concluded that the case was probably one of idiopathic amyotrophia, as described by Mya and Luisada in the *Rivista di patologia nervosa e mentale* in 1898.

The second patient, a boy of 8 years, had always shown some muscular weakness but had become strikingly worse following measles one year previously. Biopsy was done, and sections of several muscles were histologically examined. Absence of pseudohypertrophy of the muscles of the calves was regarded as tending to rule out the progressive pseudohypertrophic muscular dystrophy of Duchenne and as suggesting that the case belonged to the type of progressive muscular atrophy described by Leyden and Moebius.

In neither case was there a family history of similar muscle disorder.

HIGGINS, Boston.

DIFFERENTIAL DIAGNOSIS OF THE ACUTE MENINGO-ENCEPHALITIC PROCESSES WITH CLEAR SPINAL FLUID. M. TORELLO CENDRA, But. Soc. catalana de pediat. **5**:86, 1932.

Examination of the spinal fluid is advised to be made in the following order: microscopic examination and tests for albumin, for dextrose and for chlorides, the Nonne-Apelt test and other tests for globulin. The laboratory findings typical of each disease are outlined. For purposes of prognosis the author stresses the importance of differentiating the tubercular granuloma from tubercular basilar meningitis, the chloride content being diminished in the latter condition.

WATSON, Elmhurst, Ill.

CLINICAL ASPECTS OF NIRVANOL SICKNESS. J. M. SAA, P. CALAFELL and J. GAVIN, But. Soc. catalana de pediat. **5**:149, 1932.

Three patients with chorea were successfully treated with nirvanol. A detailed description is given of the course of the sickness caused by this drug.

WATSON, Elmhurst, Ill.

BRIEF CONSIDERATIONS OF FOUR CASES OF MONGOLISM. CLAUDI BASSOLS, But. Soc. catalana de pediat. **5**:227, 1932.

Mongolism accounts for less than 6 per cent of the feebleminded in Catalonia. It is not possible to estimate the importance of heredity. Four typical cases are reported. No treatment was successful.

WATSON, Elmhurst, Ill.

THE CAUSE OF SALAAM SPASMS. JOHANNES SCHOEDEL, Monatschr. f. Kinderh. **60**:436, 1934.

The etiology of salaam spasm is usually ascribed to epilepsy or occasionally to infections such as meningitis or syphilis. Schoedel reports two cases in which the condition obviously followed injury at birth. He uses these cases as evidence against the idea of associating the condition either with epilepsy or with congenital idiocy.

GERSTLEY, Chicago.

FAMILIAL GLIOMA (THE GENETICS OF GLIOMA). W. BENDER and F. PANSE, Monatschr. f. Psychiat. u. Neurol. **83**:253 (Sept.) 1932.

Bender and Panse report the occurrence of symptoms pointing to tumor of the brain in three brothers. Postmortem examination, which was performed in one case, revealed a glioma involving the central portions of the brain. Microscopically the tumor was rich in polymorphous and mitotic cell forms. It was regarded as belonging in the group of spongioblastoma. Histologic examination of the cerebral cortex disclosed developmental anomalies of the cyto-architecture. One of the patients observed by the authors presented a tumor of the skin which resembled adenoma sebaceum, and the others showed nevi. These features led Bender and Panse to conclude that familial glioma and tuberous sclerosis are closely related. They believe that their cases belong in the group designated by Bielschowsky as fetal spongioblastosis, which includes tuberous sclerosis, Recklinghausen's disease, familial hypertrophic neuritis and probably certain forms of epilepsy and diffuse sclerosis.

ROTHSCHILD, Foxborough, Mass. [ARCH. NEUROL. & PSYCHIAT.]

FUNDAMENTAL REMARKS ON THE PATHOGENESIS OF AMAUROTIC IDIOCY. K. SCHAFFER, Monatschr. f. Psychiat. u. Neurol. **84**:117 (Nov.) 1932.

The chief pathologic features of amaurotic family idiocy are the characteristic swelling of the ganglion cells and the filling of these cells with granules showing an affinity for hematoxylin. While similar changes occur in Niemann-Pick's disease,

here other alterations are also observed. There are foam cells and fine dustlike granular deposits of lipoid in the meninges and the walls of the vessels. These features, which are characteristic of Niemann-Pick's disease, point to a mesodermal factor that is lacking in cases of amaurotic idiocy. The signs of metabolic disorder noted in the liver, spleen and lymph glands of patients with Niemann-Pick's disease fail to occur in pure cases of Tay-Sachs' disease. The fact that ganglion cell changes are observed in cases of Gaucher's disease and of Niemann-Pick's disease does not necessarily indicate a relationship to amaurotic family idiocy. Such changes are to be regarded as a general, and not a specific, type of reaction. Here Schaffer draws an analogy from another field, pointing out that fibrillary alterations of the Alzheimer type were at first considered pathognomonic of presenile disorders, though it is now known that they may occur in conditions independent of presenility or senility. The case described by Smetana as one of splenohepatomegaly with amaurotic idiocy is excluded from the Tay-Sachs' group by Schaffer owing to the absence of macular alterations. According to Schaffer, no typical case of the infantile form of amaurotic idiocy has failed to show idiocy, macular changes and spasms. The histologic features of Niemann-Pick's disease point to a causal factor in mesodermal tissues outside the nervous system, the ectodermal alterations being secondary. In contrast to this, Tay-Sachs' disease is primarily and exclusively an ectodermal disorder, with the ganglion cells of the whole nervous system affected. The first visible alteration is swelling of the cytoplasm. Schaffer looks on this as a colloidal swelling of the hyaloplasm produced by the taking up of water. The granules are deposited or precipitated later. In the chronic juvenile form of amaurotic idiocy the tempo of the process is modified, the swelling is less marked and the deposits consist of more mature lipochrome pigment. Epstein and others have shown that a general phosphatide lipoidosis of the liver, spleen and bone marrow does not occur in Tay-Sachs' disease. The fact that Epstein was unable to find any increase in the phosphatide or cholesterol content of the brain in a case of amaurotic family idiocy indicates that the deposits are formed from substances originally present in the nervous system. The pronounced increase of lipoid in Niemann-Pick's disease owes its origin to the fact that the lipoid is brought to the brain by the histiocytic apparatus. In Schaffer's opinion, when Niemann-Pick's disease shows macular changes typical of amaurotic idiocy it represents a combination of two independent disorders, one (Niemann-Pick's disease) affecting the mesodermal and the other (Tay-Sachs' disease) the ectodermal germinal layers.

ROTHSCHILD, Foxborough, Mass. [ARCH. NEUROL. & PSYCHIAT.]

TREATMENT OF CHOREA MINOR BY HYPNOSIS. M. ESZENYI, München. med. Wchnschr. **81**:1340 (Aug. 31) 1934.

The present methods of treating chorea minor are unsatisfactory. The induction of hyperpyrexia in a weak anemic child should not be considered lightly. Even if improvement occurs after such treatment, it is usually at the time that spontaneous recovery frequently occurs. The administration of arsenic may cause intestinal disturbances, intoxication, herpes, neuritis or conjunctivitis. The therapeutic dose of phenobarbital or phenyl-ethyl-hydantoin is too near the toxic dose to make either of them a desirable drug in the treatment of chorea. The long list of sedatives which are used indicate that none of them produce satisfactory results.

It is important to decide whether chorea is an organic disease or whether it is due to some functional disturbance. It is usually considered an infection associated most frequently with articular rheumatism but at times preceded by typhoid, influenza, varicella, nephritis, scarlet fever or diphtheria. For this reason some investigators believe that it is a nonspecific infection. However, since most children have one or more of the enumerated diseases and chorea develops in relatively few, there must be some other factor involved.

Chorea affects mostly the neuropathic, anemic child, usually after some psychic injury. Eszenyi believes that there is a constitutional inferiority present in the

child in whom chorea develops. He treated ten children by hypnosis. The patients with chorea are especially susceptible to suggestion and can be brought into a somnambulant state with one or two hypnoses. The choreiform movements usually diminished immediately. They stopped sometimes after four, but always after ten, hypnoses.

BRAHDY, Mount Vernon, N. Y.

THE PSYCHOLOGICALLY NORMAL CHILD IN LIGHT OF THE PSYCHOLOGY OF PRIMITIVE PEOPLE. HEINZ WALLER, Ztschr. f. Kinderh. **55**:17 (May) 1933.

Waller finds numerous parallels between the psychologic life of primitive people and the behavior of neurotic children and comes to the conclusion that regression plays an important rôle in the psychology of the abnormal child.

LEVINSON, Chicago.

PROGNOSIS OF EPIDEMIC MENINGITIS DURING INFANCY. FRIEDRICH HASSELBACH, Ztschr. f. Kinderh. **55**:161 (July) 1933.

Hasselbach studied twenty infants suffering from meningococcus meningitis who were admitted to the University Children's Hospital in Königsberg between 1925 and 1931. Twelve of these died; six of the nine who recovered were treated by administration of antimeningococcic serum given intraspinally. The author discusses the prognosis from the standpoint of the sequelae, which consist in mental deficiency, blindness, deafness, impairment of hearing and paralysis.

LEVINSON, Chicago.

SURGICAL CONSIDERATION OF PROGRESSIVE HEMIATROPHY OF THE FACE. GEORGE BAKÁCS, Orvosi hetil. **78**:590 (June 30) 1934.

Romberg described the first case of hemiatrophy; Curshmann classified it as: (1) hemiatrophy of the face; (2) hemiatrophy of the whole body; (3) the crucial form, or atrophy of half of the face and atrophy of the contralateral half of the body; (4) bilateral facial atrophy; (5) atrophy associated with the paralysis of the cerebral nerves; (6) hemiatrophy associated with multiple sclerosis, epilepsy, hysteria and tabes dorsalis.

The disease is considered as a trophoneurosis affecting the trigeminus or the cervical sympathicus or both; it is predominant in women under 30 years of age; the left side of the face is more frequently affected. Occasionally pain in the trigeminus region precedes the hemiatrophy. It is a slow disease and starts in the skin, progressing to the subcutaneous tissue, muscle, cartilage and bone. According to Beer, in 27 per cent of the cases the etiology is neuropathic; in 44 per cent of the cases the condition follows different acute and chronic infectious diseases. In some instances trauma was considered to be responsible for the onset of the disease. Pathologically, thickening of the perineurium and diminishing of the nerve fibers of the trigeminus were found. Other authors described infiltrations by small cells in the ganglion stellatum or in the cervical ganglions of the sympathicus. In the differential diagnosis congenital hemiatrophy, atrophy due to defects of bone, to absence of teeth and to scars and, finally, sclerodermia should be excluded. As the course of the disease is undetermined, only symptomatic treatment is available. Conservative therapy with endocrine products, galvanic irritations and injections of allyl thio-urea are of questionable value. The surgical replacement of the atrophic tissues by injections of paraffin and oil is not only unsatisfactory but also dangerous. The best surgical intervention is transplantation of fat. However, even with the finest technic damage of the fibers of the facial nerve can sometimes not be avoided.

Bakács describes a typical case of hemiatrophy of the left side of the face in an 8 year old neuropathic Jewish girl. The child's third cousin suffers from hemihyperidrosis of the face. In the patient no infectious origin could be found for the hemiatrophy. The skin, subcutaneous tissue and the facial muscles were

markedly, the bones and cartilages mildly, involved. No neurologic disorder of the trigminus nerve or atrophy of the tongue was noted. The cause of the disease was thought to be some lesion around the third ventricle in the gray substance of the brain where the sympathicus centers are located.

After the disease became stationary, in about five years after the onset, transplantation of fat from the gluteal region to the face was performed with very satisfactory results. The postoperative time of observation was three years.

KERESZTURI, New York.

OCULAR COMPLICATIONS OF EPIDEMIC CEREBROSPINAL MENINGITIS. I. O. MERKULOW and I. N. MILLER, Vrach. delo **16**:702, 1933.

Merkulow and Miller made a study of the nature and incidence of ocular complications of epidemic cerebrospinal meningitis during the epidemic of Charkow in 1931. A series of 318 cases were studied. The observations were as follows:

1. Ocular complications, not including conjunctivitis, which the authors consider to be a symptom rather than a complication of meningitis, occurred in a total of 29 of 318 patients, or in 9.1 per cent of the cases.

2. The incidence of ocular complications, as well as of meningitis, is greatest at the age of 3 years or below.

3. Regarding the nature of the complications the following observations were made:

Keratitis	in 2 patients,	or 4.9%
Inflammation of the uveal tract	in 7 patients,	or 16 %
Optic neuritis	in 6 patients,	or 14 %
Paralysis of the ocular muscles	in 15 patients,	or 34.9%
Amaurosis of central origin	in 13 patients,	or 30 %

4. A certain relationship was found between the incidence and form of the ocular complications and the type of meningitic involvement. The authors distinguished three main groups of meningitis: the predominantly meningitic form, the meningo-encephalitic form and the septicotoxic form. Uveitis and neuritis were the most frequent form of complications in the predominantly meningitic form of the disease, while paralysis of the ocular muscles and amaurosis of central origin occurred most frequently in the meningo-encephalitic form.

5. Paralysis of the ocular muscles is frequently of grave prognostic significance in meningitis.

BODER, Chicago.

ORAL COMPLICATIONS OF EPIDEMIC CEREBROSPINAL MENINGITIS. M. A. ZUCKERMANN, Vrach. delo **16**:706, 1933.

A study was made of the nature and incidence of aural complications in epidemic cerebrospinal meningitis during the epidemic in Charkow in 1931. A series of two hundred and thirty cases was studied. The author's conclusions are: Acute otitis media occurred in 22.5 per cent of the cases, as compared with the figure of 50 per cent for the cases reported in the German literature. The incidence of acute otitis media as a complication of epidemic cerebrospinal meningitis was greatest before the age of 6 years, when it occurred in 78 per cent of the cases. The clinical course of early as well as of late otitis was usually uneventful, mastoiditis having occurred in only 0.8 per cent of the author's cases. Involvement of the vestibular apparatus occurred rather frequently in the author's series. Deafness, partial or complete, occurred in 3.8 per cent of the cases. As to the time of onset of the aural complications, 23 per cent occurred in the first week and 78 per cent during the second week of the disease or later. It had not been possible to isolate a meningococcus from the aural discharge, either by direct smear or by culture. Antimeningococcic serum did not seem to influence the frequency or the course of the aural complications.

BODER, Chicago.

THE COMPLICATIONS OF CEREBROSPINAL MENINGITIS. B. C. KRONZON, Vrach. delo **16**:707, 1933.

Kronzon made a study of the incidence and the character of the complications of cerebrospinal meningitis. His material consisted of 318 patients affected by the epidemic which occurred in Charkow in 1931. Under complications the author considers only those which remained present even after recovery from the original disease. His observations are as follows: Complications occurred in 54 of 318 patients, or in 18 per cent of all the patients, and in 30 per cent of the patients who recovered. Hydrocephalus was a complication in 16 cases, ocular disorders in 29, deafness and deaf-mutism in 9 and paresis and paralysis in 5. Complications occurred most frequently in the severe forms of the disease, but not in the fulminating forms. Complications were most frequent in infants and in children up to the age of 2 years. Thus, of 59 cases with complications, 34, or 63 per cent, occurred before the age of 2 years. Hydrocephalus occurred almost entirely before the age of 1 year. Early hydrocephalus is of grave prognostic significance.

BODER, Chicago.

PROGNOSIS OF EPIDEMIC CEREBROSPINAL MENINGITIS IN CHILDREN. S. M. BENDERSKAYA, Vrach. delo **16**:714, 1933.

The results of the study of fifty-one patients with epidemic cerebrospinal meningitis who received no antimeningococcic serum are reported. The author's observations are as follows:

The mortality from epidemic cerebrospinal meningitis is greater in the younger group of children. The prognosis is usually grave in the protracted form of the disease. Marked opisthotonos in infants is usually of grave prognostic significance. Increasing hydrocephalus is a dangerous sign. Generalized convulsions occurring late in the disease are of grave prognostic significance. The toxic and encephalitic syndromes are prognostically unfavorable. Vomiting occurring as a late symptom is unfavorable. A superimposed infection complicating the course of epidemic cerebrospinal meningitis makes the prognosis of the disease more serious.

BODER, Chicago.

NERVOUS MECHANISM OF OPTIC NYSTAGMUS AND ITS SIGNIFICANCE IN TOPICAL DIAGNOSIS OF CEREBRAL LESIONS. V. G. ALEKSEEVA, Vrach. delo **17**:86, 1934.

Optic nystagmus has been studied in patients with cerebral lesions. Its absence on one side (opposite to that of the lesion) was noted in cases of hemorrhages accompanied by paresis of the associated ocular movements in one case of hemorrhage in the posterior part of the internal capsula, in the case of a tumor of the temporal lobe penetrating deeply into the brain substance, in a case of tumor affecting the acoustic nerve, as well as in a case of tumor, which was situated in the posterior part of the frontal lobe and occupied all the anterior part of the parietal and the superior part of the temporal lobe, penetrating into the brain substance and reaching to the fissura longitudinalis superior. In the last case optic nystagmus to the side opposite to the lesion had been absent before the operation, after which it reappeared, but the second phase was slow. This slowness of the second phase was even more marked in another case in which optomotor nystagmus was investigated several months after the extirpation of the forepart of the right frontal lobe. The coincidence of the absence of optic nystagmus with palsy of associated eye movements compels one to assume the identity or the intimate connection of paths serving the nystagmus and those going from the frontal center of oculogyric movements; slowness of the second phase of optic nystagmus in the lesions of the frontal lobe argues in behalf of the existence here of the center of the second phase of optic nystagmus and may serve as a local diagnostic symptom for lesions of this lobe. As such a center one can assume only the field 8 or 6 a β (according to Vogt), and the deficiency of optomotor nystagmus serves as an indicator for lesions of these fields.

YAMPOLSKY, Atlanta, Ga.

SPINAL MECHANISMS OF FAT METABOLISM. N. A. POPOVA and A. E. GESKINA, Vrach. delo **17**:93, 1934.

The importance of lower (including spinal) neural mechanisms in endogenous disturbances of the fat metabolism is not sufficiently known as yet. The authors report a carefully studied case, with clinical, postmortem and histologic observations. Clinically there was the picture of amyotrophic lateral sclerosis (the polyneuritic form). The patient showed, among other disorders, the development in the subcutaneous tissue of what proved to be multiple circumscribed lipomatosis. A detailed study of this case led the authors to the following conclusions:

1. Circumscribed lipomatosis may appear in diseases of the spinal cord, probably of the gray substance. 2. Two factors play a part in the genesis of the amyotrophic lateral sclerosis: the endogenous, viz., the hereditary, and the exogenous, viz., the infectious, one. 3. In atypical cases of amyotrophic lateral sclerosis there may be a diffuse spreading of lesions.

YAMPOLSKY, Atlanta, Ga.

THE LOCAL IMMUNITY IN THE SUBARACHNOID SPACE. D. A. SHAMBUROV, A. E. KULKOV and M. E. TARNOPOLSKAYA, Vrach. delo **17**:206, 1934.

The authors describe an experimental study with a histologic control. They experimented with rabbits, which they immunized against Streptococcus and Bacillus coli, and came to the conclusion that subarachnoidal immunization provokes a local immunity which protects the animals from death after the introduction of virulent micro-organisms into the subarachnoidal space. The mobilization of all means and resources for the reduction of the infection and toxins is achieved so quickly that only transitory slight oscillations of the body temperature result, the general state of the animal remaining undisturbed. The nonimmunized rabbits perish, with an increasing fall of body temperature which denotes the unimpeded penetration in the brain tissue of the infectious agent or its toxins, which invade the vital vegetative centers of the brain.

Test rabbits used as controls which perished after the introduction of B. coli or streptococci culture into the cisterna posterior, as well as immunized animals, have been investigated histologically. These investigations confirm the data obtained experimentally and permit the conclusion that in immunized animals there is a change of the mesodermal reaction in the central nervous system. This change is noted in control animals six days after the introduction of the infection, whereas in immunized rabbits the mesodermal elements react immediately to the incubation of the noxious bacteria.

YAMPOLSKY, Atlanta, Ga.

TETANY IN INFANTS UNDER THREE MONTHS OLD. E. GORTER and J. J. DE DOES, Maandschr. v. kindergeneesk. **3**:454 (Aug.) 1934.

The authors observed seven cases of convulsions in children younger than 3 months. They discuss the possibility that the convulsions were caused by tetany and defend this conception by stating that in this condition the calcium content of the blood serum is lowered, and that it rises as the child is recovering; further, that by specific treatment the convulsions immediately disappear and do not return. The reports of the seven cases are followed by a review of the literature on the calcium content of the blood serum in young children with convulsions.

VAN CREVELD, Amsterdam, The Netherlands.

Diseases of the Eye

GLIOMA OF THE RETINA; REPORT OF A CASE WITH INTRACRANIAL EXTENSION. CARL WHEELER RAND, Arch. Ophth. **11**:982 (June) 1934.

The plea is made that in all cases of glioma the disease should not be treated as one of the eye, but that extension to the brain must be prevented by excision of as much of the optic nerve as possible and resection intracranially of the nerve as far back as the chiasm if there is any evidence of its involvement.

WESCOTT, Chicago.

THE CAUSES AND PREVENTION OF BLINDNESS. ARTHUR J. BEDELL, Bull. New York Acad. Med. **10**:593 (Oct.) 1934.

This is a detailed discussion on the cause and prevention of partial or complete blindness, including hereditary tendencies, prenatal stigmas, factors pertaining to abnormal pregnancy, obstetric accidents and postnatal conditions leading to this most unfortunate handicap. Certain optic anomalies point to a familial tendency; others appear as mere catastrophes for no particular reason. Congenital cataract is not always recognizable at birth, and the opacity may not be noticed for many months. Syphilitic effects on the eyes likewise may not make their appearance until late in childhood or shortly after puberty.

Among the postnatal infections which destroy eyesight gonorrheal ophthalmia and syphilitic keratitis are outstanding. Yet the nonsyphilitic infections which make their appearance with mucopurulent discharges are not always benign in their ultimate effects. A careful regimen must be followed to prevent chronicity and its attendant inflammatory changes.

Xerophthalmia, though infrequent, is an important cause of blindness among children whose diet is deficient in certain essential food elements. Trachoma, likewise, though less frequent than in former years, is the cause of many cases of poor vision or complete blindness in some sections of this country. Various new growths and degeneration processes of the optic nerve are important factors in the causation of blindness. Injury to the eyes during play causes loss of sight among hundreds of children annually.

The prevention of blindness is the duty of the physician. Through the constant education of parents to guard the children against accidents, hygienic measures during pregnancy, proper postnatal care, cleanliness and vigilance, not only accidents but many of the nonsyphilitic infections may be averted. Systematic treatment of the syphilitic mother during and after pregnancy, the utmost care during and following the delivery of the baby, especially if the mother has gonorrhea, early recognition and proper care of whatever anomalies or infections of the eye present themselves and intelligent treatment of injuries of the eye will save many thousands of unfortunate persons a lifetime of discouraging handicap and tragic uselessness.

JAHR, Omaha.

THE PREVALENCE OF VISUAL DEFECTS IN CHILDREN; EYE SURVEY AT ST. CHRISTOPHER'S HOSPITAL FOR CHILDREN IN PHILADELPHIA. JACOB B. FELDMAN, M. Rec. **140**:195 (Aug. 15) 1934.

From this survey it was found that (1) the easiest method of testing preschool children's vision is by the illiterate "E" chart or the method of Landolt; (2) about 50 per cent of children have a visual defect of some sort or other; (3) color blindness was present in greater amount in boys than in girls; (4) amblyopia is more common among girls than among boys; (5) manifest squints were divided equally between the sexes.

WILLIAMSON, New Orleans.

REPORT OF AN UNUSUAL CASE OF ORBITAL TUMOR. W. H. GOW, Brit. J. Ophth. **18**:520 (Sept.) 1934.

A girl, aged 18 years, had first noticed an increase in the size and prominence of the left eye when she was 12 years old. The eye was blind. There had been a gradual but slow increase in the size of the tumor. The orbit was exenterated. The tumor measured 21 cm. in circumference in its anteroposterior plane and 18.8 cm. in the lateral plane. The anteroposterior diameter was 7.5 cm., and the lateral and vertical diameters were 5.5 cm. On section it was found to be a cyst containing 90 cc. of a thick brownish fluid.

The wall in the posterior half of the cyst was fairly uniform in thickness, but in the anterior half it was thickened irregularly with the remnants of the eyeball, the thickened cornea and conjunctiva and parts of the lid. The wall of the cyst anteriorly was similar to that elsewhere, but in front of it lay the collapsed eyeball, the cornea covered by a cornified, scaly mass, and thickened lids.

The cyst originated posterior to the eyeball. The lining was composed of squamous epithelium, and the cyst was therefore an epithelial or dermoid cyst. Gow was not able to find in the literature any mention of a tumor similar to this one.

The article is illustrated. ZENTMAYER, Philadelphia. [ARCH. OPHTH.]

THE EYES AS A CAUSE OF HEADACHE. ARTHUR GRIFFITH, Brit. M. J. **2**:296 (Aug. 18) 1934.

This is a brief general discussion of the part played by ocular muscle strain and abnormality of the muscles of the eye in the causation of headaches.

ROYSTER, University, Va.

HEADACHES IN RELATION TO OCULAR CONDITIONS. WILFRED HARRIS, Brit. M. J. **2**:298 (Aug. 18) 1934.

This article is similar to the preceding one and is not adaptable to abstracting.

ROYSTER, University, Va.

TOOTH IN A LID AND PALPEBRAL COLOBOMA. VAN DER STRAETEN and APPELMANS, Arch. d'opht. **51**:417 (July) 1934.

In a boy, 5 years old, a tumor was found in the inner third of the right lower lid. At birth two teeth were present in the gums corresponding to the canine and lateral incisor on the right side. These were lost at the age of 3 weeks. The tumor of the lid was removed. Histologic examination showed it to be an uncalcified but perfectly formed tooth. There was no evidence that the tumor was a dermoid. This case is of interest because of the coincidental occurrence of a coloboma of the lid in which a tooth was found. The authors point out that coloboma of the lid is the least rare of the congenital malformations present in this case. It more commonly involves the upper lid. When the lower lid is affected, the defect occurs in the inner third and is frequently accompanied by other malformations, such as dermoid of the cornea. In order to explain the presence of a tooth in the lower lid they call attention to the derivation of the lower lid from the first branchial cleft. They also call attention to the review of the whole subject by van Duyse in the *"Encyclopédie française d'ophtalmologie."*

MARLOW, Syracuse, N. Y. [ARCH. OPHTH.]

A RARE FORM OF PERSISTENT PUPILLARY MEMBRANE WITH MICROPHTHALMOS. F. F. COSMETTATOS, Arch. d'opht. **51**:532 (Aug.) 1934.

A case is described of a microphthalmic eye in which the pupil was blocked by a cone-shaped brownish membrane attached to the pupillary margin of the iris throughout its whole circumference. This cone extended to the posterior surface of the cornea, where some fine pigment was noted. It seemed to be attached to the endothelium. An unsuccessful attempt was made to remove the membrane in toto. After a piece had been excised, the lens behind was found to be cataractous. Histologic examination of the excised portion confirmed the clinical diagnosis of persistent pupillary membrane. Cases in which a persistent pupillary membrane is attached to the pupillary margin of the iris are rare. Cosmettatos refers briefly to those which have been described in the literature and offers an explanation for the occurrence of this form. MARLOW, Syracuse, N. Y. [ARCH. OPHTH.]

BLOODY TEARS. C. DEJEAN, Arch. Soc. d. sc. méd. et biol. de Montpellier **15**:468, 1934.

The spontaneous periodic flow of "bloody tears" without apparent local cause has been occasionally observed by physicians since the seventeenth century. Gabriélidès in 1923 collected eighteen cases. The blood is not derived from

the lacrimal apparatus, as was once believed, but exudes from fine conjunctival vessels.

In Dejean's patient, a girl of 11, blood was observed sporadically to fill the culdesac of the left eye, flow over the cheek and after a few minutes stop spontaneously. No rupture of conjunctival vessels could be detected; it seemed as though the vessels became suddenly dilated and permeable. Later occurred also recurrent epistaxis, hemorrhage from the gums and subcutaneous ecchymoses. Since the conjunctival hemorrhages ceased permanently after the girl's first menstruation at 13, the "bloody tears" in this case probably represented a vicarious menstruation. In other cases, such as those of hysteria, the vasomotor changes may have been precipitated by similarly acting hormonic or sympathetic crises.

LEBENSOHN, Chicago. [ARCH. OPHTH.]

CHANGES IN THE PAPILLA OF NASAL ORIGIN. BONNET, SARGNON and PAUFIQUE, Bull. Soc. d'opht. de Paris, June 1934, p. 349.

A boy 13 years old complained that with his right eye he had been seeing many black spots in his field of vision for the past eighteen days. Visual acuity was normal. The anterior segment and vitreous were normal. The papilla presented a hazy outline; the veins were dilated, and one could observe a circle of edema adjoining the disk on the nasal side. The temporal segment was normal. The visual fields had the usual extent, but there was some constriction for colors, more especially for green. The roentgenogram of the head, the urine and the Wassermann test were normal. The right nasal passage showed signs of obstruction. The edema of the fundus increased. Several polyps were removed from the nose, and recovery was immediate.

MAYER, Chicago. [ARCH. OPHTH.]

BRIDGES OF THE SELLA TURCICA. K. VELHAGEN JR., Arch. f. Augenh. **108**:559, 1934.

In certain cases, atrophy of the optic nerve, especially that thought to be due to a form of glaucoma without demonstrable rise in tension, has recently been described in the literature as due to certain variations in the bones of the skull. The bony bridges which are occasionally found over the sella are a type of such changes. In order to determine their frequency among persons who show no optic nerve changes, Velhagen examined the skulls in the anatomic museum and x-ray films of skulls taken in the pediatric service of the hospital. Children's skulls were selected in order to avoid the changes due to senile calcification. He found that as high as 10 per cent of the skulls showed these bridges and concludes from this that they probably have little pathologic significance and are merely coincidental findings in the cases of "pseudoglaucoma."

ADLER, Philadelphia. [ARCH. OPHTH.]

SUN-FLOWER CATARACT IN HEPATOLENTICULAR DEGENERATION (PSEUDOSCLEROSIS): REPORT OF A CASE. R. THIEL, Klin. Monatsbl. f. Augenh. **93**:12 (July) 1934.

A boy, aged 15, had been well up to his twelfth year, when he had several attacks of fainting, with unconsciousness lasting for about ten minutes, and symptoms which aroused suspicion of typhoid fever; these, however, disappeared after ten days. The swelling of the liver and spleen noted at that time persisted. A year later he presented cramps of his right hand and of virtually his whole body, though more in the left side than in the right side, and rigidity of the platysma myoides, pulling the left angle of the mouth extensively to the left side. In the course of the disease, tonic spasms of all the muscles developed, which occurred spontaneously or were instigated by voluntary motion. Besides these extrapyramidal disturbances of motility, a severe lesion of the liver was present, completing the picture of hepatolenticular degeneration, viz., pseudosclerosis. The following ocular symptoms were observed: (1) the Kayser-Fleischer pigment ring in Descemet's membrane and (2) a faint opacity in the anterior capsule of the lens with

short radiating extensions typical of a sun-flower cataract. Noticed originally in the presence of copper in the globe only (chalkosis of the lens), sun-flower cataract was found also in pseudosclerosis by Siemerling-Oloff and Vogt. This so-called "apparent cataract," seen only in transillumination, showed a distinct yellowish hue and opalescence, while the radiating extensions, arranged a short distance from the opaque central disk, presented a bluish-green hue. The lens of the right eye was not removed, as the vision of the left eye was normal. No change of the ocular symptoms occurred within one year's observation.

STOLL, Cincinnati. [ARCH. OPHTH.]

PATHOLOGIC ANATOMY OF ALBUMINURIC NEURORETINITIS: REPORT OF A CASE. E. WÖLFFLIN, Klin. Monatsbl. f. Augenh. **93**:446 (Oct.) 1934.

A man, aged 58, with chronic nephritis and alcoholism, noticed severe failure of vision for a year prior to observation. The disks were congested; numerous retinal hemorrhages and white foci were noticed, but no star-shaped figure. Later on, increase of the white foci obscured the view of the left disk. The retinal veins were but slightly distended. The pathologic changes in the globes are described and discussed in detail.

The presence of many large cysts in the retina is explained as resulting from chronic and extensive hypertension of the arteries. These cysts resembled the vacuoles of Iwanov and were deemed to be outgrowths of physiologic degeneration, which occurred simultaneously. Glaucoma did not develop as a result of the hypertension in the retinal arteries because, in Wölfflin's opinion, the affluent flow equaled the defluent flow. In this connection, he puts the question: Why is edema of the retina never observed in glaucoma with high tension? Simple hypertony of the central retinal artery cannot produce glaucoma unless other changes, such as atrophy of the iris and obliteration of the angle of the chamber, obstruct the defluent flow. Hence glaucoma is never found with albuminuric retinitis except as a rare complication. The white foci in the retina according to Wölfflin, represent an extensive edema and also proliferations of the neuroglia or accumulations of lipoid substances, varicose degenerations of the nerve fibers and occasionally deposits of fibrin. The hypertrophies in the retina and choroid are considered as a result of the increased arterial pressure. The retinal cysts contained either a transparent liquid or a very fine network. Fibers of the latter could be followed into the retinal tissue, suggesting that they were remnants of the intergranular layer. A peculiar misplacement of the layers of the retina and distinct hypertrophy of the neuroglia on the left disk may have been caused by inflammatory or toxic processes.

STOLL, Cincinnati. [ARCH. OPHTH.]

SEVERE FATAL OSTEOMYELITIS OF BOTH ORBITS: REPORT OF A CASE. H. PUSCARIU and D. LAZARESCU, Klin. Monatsbl. f. Augenh. **93**:531 (Oct.) 1934.

The authors give a synopsis of the literature in point and details of the differential diagnosis and etiology. Then they report the case of a child, aged 2½ years, who was admitted to the hospital with bilateral exophthalmos, which had developed about six months after an attack of measles. The progress of the disease was slow; no cause was known; high fever was absent; the general physical condition had been satisfactory. Increase of the exophthalmos, the only symptom for a long time, suggested inflammation of the tissues of both orbits. Pus was found after opening the ethmoid sinus. Despite this procedure the infection involved the orbital walls, spread into both antrums and caused multiple abscesses containing staphylococci. Death resulted from an accumulation of pus which separated the dura mater from the cranium and pushed the brain into the anterior portion of the skull. A roentgenogram had suggested the presence of a tumor. The brain remained free from infection, as the dura mater formed a wall against the entrance of the infected pus.

STOLL, Cincinnati. [ARCH. OPHTH.]

A Rare Case of Congenital Hydrophthalmos. A. A. Bielsky, Sovet. vestnik oftal. **5**:579, 1934.

A child, aged 2½ years, had typical bilateral hydrophthalmos. The unusual feature was the periodic spontaneous dislocations of the lenses into the anterior chambers and their disappearance within from several hours to two days. The luxations sometimes occurred alternately and sometimes simultaneously. The dislocated lens was always located at or a little below the pupil, but never did it sink to the bottom of the anterior chamber. It seemed as though the lens was attached posteriorly (to hyaloid membrane ?). It was impossible to produce the dislocation of the lens artificially. The possible explanation that Bielsky gives is that the increase of the intra-ocular tension pushed the lens forward; when, owing to some changes in the endocrine vegetative apparatus, the tension decreased the lens was drawn back into the posterior chamber. Myotics did not change the condition.

Sitchevska, New York. [Arch. Ophth.]

The Relationship Between Photophobia and Nyctalopia. Shimizu, Acta soc. ophth. jap. **38**:83 (June) 1934.

The vision of patients with albinism and aniridia who were suffering from corneal ulceration or iritis was examined under various degrees of illumination. Shimizu found that with increased illumination vision improved notwithstanding the unpleasant feeling which the additional light produced. In other words, the results were quite different from those found in diseases which produce nyctalopia.

Knapp, New York. [Arch. Ophth.]

Familial Hereditary Optic Atrophy. K. T. A. Halbertsma, Nederl. tijdschr. v. geneesk. **78**:4079 (Sept. 8) 1934.

After an introduction on the history and nature of familial hereditary optic atrophy an exposition of the mode of heredity and the familial character of this disease is given. Starting from the data in the literature of The Netherlands, which is reviewed, the differential diagnosis and some of the assumptions on the cause and nature of the disease are discussed. A number of pedigrees are considered, one of which had been traced by the author, and on the basis of these the relations of heredity are considered. In four of the five pedigrees the inheritance appears to be typically recessive sex-linked, whereas in the remaining one probably a change of dominance has to be assumed. In the last case after a rather acute onset in a relatively short time (from eight to nine months) recovery of vision ensued. The atrophy of the papilla, however, as in all the other cases discussed, was lasting. Complications of the central nervous system, as well as other complications, were absent.

van Creveld, Amsterdam, Netherlands.

Diseases of the Ear, Nose and Throat

Argyria Nasalis. La Fayette P. Monson, Arch. Otolaryng. **19**:582 (May) 1934.

General discoloration of skin from prolonged silver medication is not infrequent, but local argyria is rare. The eye is most often involved, and the condition has been reported in the mouth, nose and in localized areas of skin. Monson cites two cases in which the condition followed the prolonged use of mild protein silver and reports a case in which a 1 per cent solution of strong silver solution was used for some years in the nose. Of particular interest is the report that the nasal interior showed a bluish-green color throughout the cavity proper only. There was no stippling of the white cells, and no polychromatophilia was seen in the blood picture. No colorimetric examination was done. Microscopic examination

showed that the outer layers of the nasal stroma contained excessive silver pigment both as fine granules and strands, occurring sometimes in phagocytic cells and also free in the tissue.

GREENWOOD, Chicago.

RUPTURE OF SUPPURATIVE CERVICAL GLANDS INTO THE EXTERNAL AUDITORY CANAL. HARRY ROSENWASSER, Arch. Otolaryng. **19**:610 (May) 1934.

Perforation of the external auditory canal by parotid abscesses is not uncommon, but perforation by pus from suppurating glands in the upper anterior cervical region is rare. Of pediatric interest is the citation that suppuration of glands in children frequently follows pharyngeal sepsis and especially pharyngeal tonsillitis. This is true for children near the age of 2 years.

Politzer stated that recent investigations have shown that the lymphatics of the anterior and superior portions of the walls of the canal, the tragus and the surrounding parts drain into the preauricular nodes (on the parotid); that those of the lobule, helix and inferior wall of the meatus empty into the infra-auricular glands (at the angle of the jaw); that those of the anthelix and concha empty into the mastoid glands (on the apex of the mastoid bone), and that those of the posterior wall of the meatus, together with those of the eustachian tube, empty into the deep cervical glands and retropharyngeal glands.

In children up to 4 years of age the osseocartilaginous attachment of the external auditory canal is loose, fibrous connective tissue. With age this becomes denser. This is one reason why these abscesses perforate here in children and rarely do so in adults.

Rosenwasser presents four cases. In the first case, pressure over the lateral wall of the pharynx produced pus through a fistula in the floor of the canal. In the second case, there was a purulent discharge from suppurating glands at the angle of the jaw through a fistulous opening in the floor of the canal at the osseocartilaginous junction. In the third and fourth cases, there were the complications otitis media and mastoiditis. The suppurating cervical glands drained through fistulous openings through the anterior and inferior walls of the external auditory canals. All these patients were under 3 years of age.

The author favors conservative treatment. The physician should use meticulous care in cleansing the canals.

GREENWOOD, Chicago.

TEMPERATURE AFTER MASTOIDECTOMY. HENRY P. JOHNSON, Arch. Otolaryng. **19**:660 (June) 1934.

Johnson reports one hundred cases. He states that the clinical thermometer came into general use in 1870. Wunderlich, in a treatise written in 1868, "found fever a disease and left it a symptom."

In the first twenty-four hours 60 per cent of the patients showed an initial drop in temperature, with subsequent elevation occurring in uncomplicated cases. Johnson concludes that postoperative fever of moderate range is customary and that it has no significance without other symptoms.

He reports four cases with preoperative complications: two with meningitis, one with nephritis and one with gastro-intestinal disturbance.

Postoperative fever was caused by: (1) otitis media and mastoiditis in the opposite ear (most common); (2) involvement of the mastoid wound (stitch abscess, cellulitis, erysipelas); (3) cervical adenitis; (4) infections of the respiratory tract (bronchitis, acute follicular tonsillitis); (5) infection of the lateral sinus in from 3 to 6 per cent of the operative cases in mastoiditis, which if seen early is remedied by simple removal of infection; (6) pyelitis, acute exanthems and septicemia with distant focal infection.

Sixty-six per cent of the patients showed a decrease in temperature from six to twelve hours after operative intervention, and twenty-eight showed an elevation in temperature. Eighty-six per cent showed an elevation in temperature in from twelve to twenty-four hours after operation, and 8 per cent showed a decrease.

Six per cent of the patients were afebrile both preoperatively and postoperatively. Sixty per cent showed no complications; 4 per cent showed preoperative otitic complications, while postoperative complications developed in 36 per cent. The febrile period averaged five days in uncomplicated cases; the greatest elevation in temperature in 80 per cent of these cases occurring in the first twenty-four hours. The postoperative temperature in cases of preoperative complications was of no special diagnostic interest. In only four of the thirty-six cases with preoperative complications were these serious. An elevation of the temperature curve was the first warning of existing complications in more than 86 per cent of the cases. Two deaths occurred.

GREENWOOD, Chicago.

LABYRINTHITIS AND SINUS THROMBOSIS COMPLICATING SUPPURATION OF THE MIDDLE EAR. JOSEPH G. DRUSS, Arch. Otolaryng. **19**:671 (June) 1934.

Druss states that labyrinthitis and sinus thrombosis complicating otitis media are more frequent than is suspected. These complications may be independent of each other, each being caused by infection of the middle ear. When one is the direct cause of the other, thrombosis of the sigmoid sinus is usually secondary to labyrinthitis.

Infection of the labyrinth may spread to the sigmoid sinus along preformed as well as along newly formed pathways. The saccus endolymphaticus and the labyrinthine veins are the most common of the preformed routes. Newly formed pathways consist of fistulas from within the labyrinth through the semicircular canals or through the body of the labyrinth. Infection spreads via the ductus endolymphaticus and the sac which lies between the layers of dura on the posterior surface of the petrosa, between the medial border of the sigmoid sinus and the internal auditory meatus, may produce sinus phlebitis or thrombosis, extradural abscess, meningitis or cerebellar abscess. The labyrinthine veins which empty into the inferior petrosal sinus or the jugular bulb are pathways for infection. The cavernous sinus may be involved via the inferior petrosal sinus.

Newly formed routes are fistulas of the semicircular canals and secondary fistulas of the body of the labyrinth. Infection may be spread by direct contiguity via osseous necrosis between the labyrinth and sinus. The posterior semicircular canal is usually the one from which infection spreads. Attention is called to the fact that fistulas here form from within outward, in contradistinction to the usual route from without inward.

Two cases are presented. The first demonstrated the two complicating lesions, probably independent of each other; the second showed the sinus involved secondary to the labyrinthitis. In both instances the running ear was involved through the fenestra ovalis (the fenestra rotunda also in case 2), while the jugular bulb in the second case was a direct route through the floor of the tympanum. Pneumococcus type III was the organism in both cases.

GREENWOOD, Chicago.

CHANGES IN THE LYSOZYME CONTENT OF THE NASAL MUCUS DURING COLD. ANDERSON HILDING, Arch. Otolaryng. **20**:38 (July) 1934.

Lysozyme is a bacteriolytic ferment found normally in the body tissues and their secretions. Hilding reports seven cases of the so-called common cold which he studied in an effort to determine the lytic power of this enzyme normally present in the nasal mucus.

Samples of nasal secretion were collected daily or more often. The Sarcina group was used for determining the lytic action of the mucus. Symptoms and signs of the patient were observed as the controlled tests in vitro proceeded. Conclusions need further support but point to a sharp reduction in the natural antiseptic properties of the nasal secretion during and preceding the invasive stage in some cases. Three patients showed a marked loss in power to destroy bacteria by lysis coexistent with marked symptoms of the infection of the upper

respiratory tract. A definite general improvement was preceded by an increase of the lytic power of the nasal secretion. The change of lysozyme content of the nasal mucus was not due to any dilution phenomena. GREENWOOD, Chicago.

DIAGNOSTIC DIFFICULTIES IN THE CONVALESCENT STAGE OF MASTOIDECTOMY. MORRIS A. WEINSTEIN and LEWIS MERKLIN, M. Rec. **140**:196 (Aug. 15) 1934.

Weinstein and Merklin give the following summary of their paper:

The temporal bone may be the seat of great danger, particularly in the postoperative stage. When symptoms point to possible complications one should first eliminate by careful examination any possible focus in the operative field. One should not be too hasty to reoperate on small children, because as a rule they present mostly the acute cases, with toxemias as a predominating factor; meddlesome surgery is not only useless but often dangerous. Adolescents and adults present more chronic pathologic conditions and require a more radical approach in appraising them. One should study carefully the patient, his general appearance and his psychic reactions. Much depends on the experience and common sense of the surgeon, for which no rule can be laid down.

WILLIAMSON, New Orleans.

METHODS OF TESTING AND MANAGEMENT OF THE DEAFENED SCHOOL CHILD. EDMUND PRINCE FOWLER, New England J. Med. **211**:364 (Aug. 23) 1934.

Fowler explains the use of audiometer testing of hearing (mass testing) in school children. The great advantage of the audiometer is that losses of both air conduction and bone conduction may be estimated in the same units of measure (the sensation unit or its equivalent, the decibel).

It can be definitely shown by repeated careful otolaryngologic examinations and audiometric tests that, if properly managed, more than 60 per cent of all children sent following school surveys can be benefited, and that lapses in treatment and management are frequently accompanied by tragic results as to the hearing and also the health.

GENGENBACH, Denver.

THE STORY OF TRACHEOTOMY. E. W. GOODALL, Brit. J. Child. Dis. **31**:167 (July-Sept.) 1934.

This, the first instalment of a historical review of tracheotomy, treats of the subject from the time of Fabricius of Aquapendente, when the operation was known as "the scandal of surgery," up to the second quarter of the nineteenth century.

LANGMANN, New York.

AN ANALYSIS OF OVER FOUR THOUSAND CASES OF EDUCATIONAL DEAFNESS STUDIED DURING THE PAST TWENTY-FIVE YEARS. MACLEOD YEARSLEY, Brit. J. Child. Dis. **31**:177 (July-Sept.) 1934.

The total number of children analyzed in this study was 4,314, comprising 2,164 boys and 2,150 girls. These were grouped into those with congenital deafness and those with acquired deafness. The present section of the article concerns only the group with congenital deafness. The data for these are given in the table:

	Boys	Girls
Hereditary	95	115
Sporadic	548	479
Aphasia	27	20
Total	670	614

Hereditary deafness is defined as that in which the family history shows other persons born deaf either in direct line or in collateral branches. The study of family histories of hereditary deafness shows definitely that hearing appears to

be the dominant, and deafness the recessive, character. Nearly all the cases of hereditary deafness in this series illustrate two salient points in mendelianism; the origin of recessives from impure dominants and the "breeding true" of pure recessives. Among the 210 patients analyzed only 11 showed consanguinity (there were 6 instances of the marriage of first cousins, 3 of the marriage of second cousins and 2 in which the degree of cousinship was not stated).

Sporadic deafness at birth is defined as that in which the family history is deficient in other relatives born deaf, save in the same generation, but may contain instances of other defects, mental or physical. In this group there may possibly be instances in which the deafness was acquired in early life and the defect was not detected until as late as the second year of life. When consanguinity is considered in this connection it seems to resolve itself largely as a matter of stock. If the stock is good and free from taint of hereditary deafness there is no reason why the offspring of a consanguineous marriage should show deafness. There were 22 cases of sporadic deafness, in 19 of which there had been marriage of first cousins and in 1 marriage of second cousins; in 2 the degree of consanguinity was not stated. Illegitimacy does not seem to play a significant rôle. Congenital syphilis and intestinal toxemia are also mentioned as possible causes of occasional instances of deafness at birth.

LANGMANN, New York.

LARYNGEAL INTUBATION. AGUSTIN FERNANDEZ LAGOS, Rev. chilena de pediat. **5**:413 (Aug.) 1934.

Intubation is indicated in most cases of true croup. The outcome is uniformly favorable in the benign nontoxic form. The dangers increase with the toxicity of the disease and the length of time it has been present. Intubation requires more careful supervision by a trained and competent personnel than tracheotomy does. The author believes the optimal time for removal of the tube to be from fifty-six to sixty hours.

SCHLUTZ, Chicago.

ULCUS VULVAE IN A CHILD FOLLOWING TONSILLECTOMY. KARL STEINER, Dermat. Ztschr. **69**:220 (July) 1934.

Following tonsillectomy a 9 year old girl had a rise in temperature to between 39 and 40 C. (102 and 104 F.) for six days. Two days after the operation an acute ulceration of the vulva appeared. Smears showed gram-positive cocci, numerous fusiform rods and spirochetes. The lesion healed rapidly. The ulceration was considered to be a metastatic lesion from an infection in the tonsillar area.

TAUSSIG, San Francisco. [ARCH. DERMAT. & SYPH.]

SYMPTOMATOLOGY OF STUTTERING. E. FRÖSCHELS, Monatschr. f. Ohrenh. **68**:814 (July) 1934.

Fröschels discusses the historical aspects and the recent studies and theories of the symptomatology of stuttering. He feels that investigations along the lines of psychoanalysis and individual psychology offer almost unlimited opportunity for a further clarification of the symptomatology of stuttering.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

BLOODLESS REMOVAL OF FOREIGN BODIES FROM THE TRACHEA OF CHILDREN. I. E. DAWYDOW, Monatschr. f. Ohrenh. **68**:936 (Aug.) 1934.

Dawydow has used the laryngoscopic method of Siefert for the removal of foreign bodies from the trachea. He regards the use of local anesthesia as a great advantage. He has employed this method on fifteen patients with a variety of foreign bodies which had been in the trachea for periods varying from three days to one and a half months. The method is also a useful diagnostic aid in determining the presence of a fixed foreign body in the trachea. No bad results were obtained

by the use of this method, and even in children in whom signs of bronchopneumonia existed the removal of the foreign bodies was followed by a rapid return to normal of the affected lung.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

OTITIS IN INFANCY. LOTAR HOFMANN, Wien. klin. Wchnschr. **47**:434 (April 6) 1934.

Hofmann remarks that the treatment of acute otitis in infancy must be general as well as local. The general treatment consists of rest and nursing care; it is often neglected in the belief that local illnesses must be treated locally. If neglect of general treatment has a harmful effect on otitis in adults, it has a still worse effect in children. Often otitis will not yield to local treatment, and it is observed that the child is feverish, restless at night and in poor general condition. If the child is taken to the hospital it is surprising how, with rest and nursing care, the poor local and general conditions improve. The local treatment depends on the progress of the otitis. In the first twenty-four to forty-eight hours no special measures need be taken, except if there are unusual indications such as meningism. Local, lukewarm instillations of phenol in glycerin may be given, and small doses of aminopyrine may be given internally. A good, though expensive, preparation is phenyl dimethyl pyrazolon. If the otitis is not severe these measures may suffice; otherwise, paracentesis must be carried out. The author believes this to be a valuable measure, although some physicians are strongly opposed to it. Paracentesis must be undertaken above all in cases of high fever and marked involvement of the tympanic membrane. The fact that paracentesis does not always cause the fever to abate does not diminish the value of this procedure, because usually there is a prompt fall in temperature as well as abatement of other symptoms. That the fever does not always disappear is due to various causes. The paracentesis causes drainage of material from the tympanic cavity and only partially from other parts of the ear and from the mastoid process. If some obstacle, such as a swelling of the mucous membrane, prevents drainage of pus from the antrum mastoideum to the typmpanic cavity, a fall of temperature is prevented. It is possible that not much pus may be present, especially if the inflammation is phlegmonous. This possibility must be kept in mind when paracentesis is undertaken too soon. If there is no pus present the opening made by the paracentesis may close, and the procedure may have to be repeated. Another cause of persistent fever after paracentesis may be the presence of some other illness such as pneumonia. After paracentesis free drainage must be obtained either by rinsing or by small gauze strips introduced daily into the ear to the tympanic membrane. If the suppuration becomes fetid, the auditory canal must be kept dry by introducing boric acid after the canal has been cleaned. If mastoiditis develops operative treatment must be undertaken.

ABT, Chicago.

CLINICAL BACTERIOLOGY OF THE POSTNASAL SPACE: I. TECHNIC. I. JUNDELL, Acta pædiat. **15**:279 (June 5) 1934.

In a previous paper published in the Swedish language in 1898 Jundell demonstrated that the subglottic portion of the respiratory tract is normally sterile or at least relatively free from bacteria; it frequently remains so during the course of acute bronchitis. A special technic was employed in these investigations. As a preliminary to further studies currently projected, the author describes in detail new instruments which he has devised for taking bacterial cultures from the postnasal space. With these instruments it is possible to avoid contamination with flora from the mouth and pharynx.

MCCUNE, New York.

ULCERATION OF NOSE AND FACE CAUSED BY MYCOSIS FUNGOIDES. E. BEHR, Nederl. tijdschr. v. geneesk. **78**:2197 (May 19) 1934.

In the literature a number of cases of a peculiar granuloma of the nose and the surrounding region, leading to extensive necrosis and gangrene, are reported.

Some cases were diagnosed as those of mycosis fungoides; in other cases an allied process was assumed, whereas in some cases a new name was invented (granuloma gangraenescens, Kraus). An analogous condition is recorded in a boy of 12 years, who came to the hospital with the complaint of abdominal pain. Shortly afterward ulceration of the nose began, and all therapeutic measures failed to bring relief. Seven months later the boy died. In all these cases the peculiar condition may be attributed to infection with mycosis fungoides; this is based on the histologic picture, the findings on other parts of the skin and the lesions of the internal organs, which fully correspond to those found, especially in the liver, in typical cases of mycosis fungoides. Though these cases retain a special position by reason of their clinical picture, there is no real reason why the condition should not be regarded as due to mycosis fungoides.

VAN CREVELD, Amsterdam, Netherlands.

REMOVAL OF FOREIGN BODIES FROM THE LOWER AIR PASSAGES WITH THE AID OF THE HASLINGER BRONCHOSCOPE. P. G. GERLINGS, Nederl. tijdschr. v. geneesk. **78**:3546 (Aug. 4) 1934.

Gerlings describes the procedure of Haslinger and discusses the advantages of this method over others, especially the method of Brünings, which was used formerly. He describes the excellent results obtained with the bronchoscope used by Haslinger in twenty-four cases of foreign bodies in the lower air passages; with one exception all the cases were those of children under 3 years of age.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of the Skin

DERMATOMYOSITIS. V. P. SYDENSTRICKER and D. R. THOMAS JR., Ann. Int. Med. **8**:959 (Feb.) 1935.

Sydenstricker and Thomas report a case of dermatomyositis in a boy aged 14. The course of the disease was acute but benign. Clinically there was a close resemblance to trichinosis. An extreme degree of eosinophilia was noted, the percentage of eosinophils ranging from 10 to 60. No cause was found to explain the eosinophilia.

READING, Galveston, Texas.

THE DEXTROSE AND WATER CONTENT OF NORMAL AND OF INFLAMED SKIN. DONALD M. PILLSBURY and GEORGE V. KULCHAR, Arch. Dermat. & Syph. **30**:489 (Oct.) 1934.

The article describes experiments on the skin of rabbits analyzed for the dextrose and water content. Studies were made on normal and inflamed skin of (1) animals receiving normal diets and (2) animals receiving injections of large quantities of dextrose. Pillsbury and Kulchar found the water content of inflamed skin to be only slightly higher than that of normal skin, the difference being 4 per cent or less. The dextrose content of the skin, with or without irritation, of animals receiving normal diets, did not vary beyond values of experimental error. The dextrose content of the inflamed skin after injection of dextrose varied from the normal and was generally higher than normal. An important observation in these experiments was that irritated areas of the skin became infected much more frequently in rabbits receiving dextrose than in those receiving normal diets. This observation is now under further investigation.

DULIN, Iowa City, Iowa.

URINARY PROTEOSE IN ECZEMA. THEODORE CORNBLEET and MORRIS A. KAPLAN, Arch. Dermat. & Syph. **30**:497 (Oct.) 1934.

Proteose was precipitated from the urine of patients with eczema, persons with nonallergic conditions and normal persons. The proteose isolated was used in various cutaneous tests, and efforts were made to immunize rabbits and to make

use of the compound therapeutically. Cornbleet and Kaplan were unable to confirm the original report of Oriel and Barber that urinary proteoses excreted by patients with allergic disorders contained specific antigens. Details of the procedures used to precipitate the proteose are given. DULIN, Iowa City, Iowa.

DANLOS SYNDROME ASSOCIATED WITH CONGENITAL LIPOMATOSIS. NORMAN TOBIAS, Arch. Dermat. & Syph. **30**:540 (Oct.) 1934.

Tobias reports the case of a girl, aged 9 years, who had the tetrad of symptoms of the Danlos syndrome, namely: (1) hyperelasticity of the skin; (2) hyperlaxity of the joints; (3) fragility of the skin, involving especially the exposed surfaces and prominences, and (4) pseudotumors following trauma. Pictures illustrating all the symptoms and a photomicrograph showing the increase in elastic tissue of the corium accompany the article. A clinical description of the case and of the pathologic processes is given in detail. Associated with the Danlos syndrome the patient had a second congenital defect, namely lipomatosis.

DULIN, Iowa City, Iowa.

A CRITICAL REVIEW OF 170 CASES OF URTICARIA AND ANGIONEUROTIC OEDEMA FOLLOWED FOR A PERIOD OF FROM TWO TO TEN YEARS. ARTHUR I. FINK and LESLIE N. GAY, Bull. Johns Hopkins Hosp. **55**:280 (Oct.) 1934.

One hundred and seventy cases of urticaria and angioneurotic edema studied for from two to ten years are reported. Information on the progress of each patient has been obtained during the past two months. The cases can be divided into five simple groups according to the etiology, as follows: (1) urticaria associated with infection; (2) urticaria associated with foods, drugs and other extrinsic factors; (3) urticaria dependent on psychogenic disturbances; (4) urticaria due to disturbances of function of the ovaries, thyroid or other endocrine glands, and (5) urticaria of undetermined cause.

Of the entire series 69 patients were females and 31 were males. Twenty-eight per cent of the patients stated that they had allergic phenomena, but personal history of allergy was of no significance. Eosinophilia was not noted.

Fifty-two cases were associated with infections; in 74 per cent of these permanent relief was obtained by removal of the infected tissue.

Thirty-five cases were due to allergic factors; avoidance of the specific cause permanently relieved these patients of their urticaria.

Treatment of the psychogenic group was less satisfactory. It is our belief that the psychiatrist is far more helpful to these patients than the allergist.

The group of patients with disturbance of endocrine function responded satisfactorily, the response depending on nature's physiologic adjustment or on administration of small doses of thyroid extract.

We have little to suggest concerning the cause or treatment of the urticaria of undetermined cause; with further study the number of patients in that group will undoubtedly be reduced.

The average duration of symptoms in the entire series before consultation was about four years; the average period of observation since consultation was three and seven-tenths years.

In conclusion, it is our belief that a more optimistic prognosis can be entertained provided a more careful diagnostic study of each patient is made with less emphasis on the importance of allergy per se. AUTHORS' SUMMARY.

ACRODYNIA WITH QUADRIPLEGIA. DEBRÉ, MARIE and MESSIMY, J. de méd. de Paris **54**:1044 (Dec. 6) 1934.

The case of a girl aged 3 years is reported. The typical signs of acrodynia developed on Nov. 15, 1933; the hands and feet were red, cold and covered with sores; the patient was uncomfortable and irritable and showed some diminution of

the tendon reflexes and slight muscular hypotonia. Two months later there developed a marked flaccid quadriplegia with total loss of the tendon reflexes and hypotonia and flabbiness of the muscles. Fluid obtained by lumbar puncture showed an increase in albumin content but no cellular increase. The quadriplegia reached its maximum in the course of three weeks and then regressed rapidly. An atelectasis of the right lung occurred after a spell of choking. This regressed slowly with no special treatment. Six months after the onset, except for the slight redness of the palms and soles, the child had completely recovered.

LESLIE, Evanston, Ill.

ACRODYNIA. C. ROCAZ and J. BOISSERIE-LACROIX, Paris méd. **1**:77 (Jan. 26) 1935.

The consensus at present concerning acrodynia is that it is due to infection with a neurotropic virus. The increase in lymphocytes and albumin content in the cerebrospinal fluid early in the disease points to such a causative agent, and Kernohan and Kennedy found degeneration of the basal nuclei in a patient examined at autopsy two hours after death. The close relationship between some of the symptoms of acrodynia and those of encephalitis and poliomyelitis point to the probability of a similar infectious basis.

Two cases are reported. The first child, in addition to the usual symptoms of acrodynia, showed an excessive thirst, drinking from 2 to 4 liters of water a day, and also had convulsive seizures. The second child showed marked change in personality, convergent strabismus and loss of speech and reflexes. Both patients recovered.

LESLIE, Evanston, Ill.

THE TREATMENT OF ECZEMA IN CHILDHOOD. J. T. RUBIO and F. RODRIGO PALOMARES, Pediatría españ. **23**:327 (Oct.) 1934.

In the treatment of eczema, Rubio and Palomares advise against the use of hot baths, and against vaccination for smallpox, on account of the danger of a generalized vaccinia. They also advise against the use of autotoxins and serums on account of the danger of severe reaction due to serum. When the urgency of the case requires the use of serums desensitization according to the method of Besredka should be practiced.

The authors advise against hospitalization of the eczematous child on the ground that he is much more exposed to infection in the institution. They also advise against all forms of vigorous local treatment.

SCHLUTZ, Chicago.

Miscellaneous

THE STUDY OF THE HIP JOINT FROM THE STANDPOINT OF THE ROENTGENOLOGIST. L. B. MORRISON, Am. J. Roentgenol. **28**:484 (Oct.) 1932.

Morrison describes the development of the hip joint from birth to adult life, with roentgenograms showing the changes at yearly periods. Tuberculosis, congenital condition of the hip, osteomyelitis and other disorders are discussed and illustrated. In addition to the usually described centers of ossification the author describes a genetic center located on the superior acetabular rim, principally in the ilium. About the twelfth year this genetic center normally forms a true epiphysis on the superior acetabular margin and is most essential in the formation of a competent hip joint. Congenital condition of the hip is the result of a retardation in the growth or a total lack of this genetic center. Early congenital condition of the hip can be diagnosed by (1) long and shallow sockets, (2) the fact that the portion of the acetabulum above the epiphysis is slightly elongated and much more shallow and (3) the fact that the femoral head, judged by means of the upper end of the diaphysis, lies above the level of the Y cartilage. Eighty roentgenograms are included.

STULIK, Chicago.

EDUCATION OF THE CHILD'S BODY—PREVENTION OF POSTURAL DEFORMITIES. REGINALD H. WIGGINS, Arch. Pediat. **51**:477 (Aug.) 1934.

Wiggins lists eighteen measures which are valuable in the prevention of postural deformities and discusses each in detail. It is believed that modern education aims at the education of the mind, leaving the education of the body to ignorance and chance.

WADDELL JR., University, Va.

FIVE YEAR FOLLOW-UP REPORT OF AN INFANT WELFARE CLINIC. GEORGE F. MUNNS, Illinois M. J. **65**:523 (June) 1934.

In a report of the results of observations on a group of children aged from 2 to 6 years, most of whom had been under supervision in clinics for infant welfare since birth, Munns states that the physical status of the group indicates that modern pediatric knowledge as applied to groups of children under care in free clinics produces satisfactory results, as evidenced by the uniform good health, low incidence of serious illness, low mortality and absence of significant or serious physical defects among them.

BARBOUR, Peoria, Ill.

ADOPTION PRACTICES AND THE PHYSICIAN. R. L. JENKINS, J. A. M. A. **103**:403 (Aug. 11) 1934.

Physicians should familiarize themselves with the factors determining good adoption practice and wherever possible should cooperate with careful child-placing agencies. Placement for adoption should be permitted only if a satisfactory arrangement for maintaining the child with one of its parents is impossible. Under such circumstances careful investigation of the home into which the child is to go should be made. The motive prompting the desire to adopt, the health of the prospective parents, with especial attention to venereal disease and tuberculosis, and the personality defects should be noted, as well as their ability to provide the security and advantages usual to the community. The child must appear suitable for adoption, and the family history, developmental history, physical behavior and the results of psychologic examination carefully considered. Legal adoption should be permitted only after a probation period of at least a year reveals a reasonably satisfactory parent-child adjustment. Children not suitable for adoption may be cared for in boarding homes suitably supervised or in institutions.

BONAR, Salt Lake City.

THE CARDIAC IRREGULARITIES PRODUCED BY EPHEDRINE AND A PROTECTIVE ACTION OF SODIUM BARBITAL. WALTER J. MEEK and M. H. SEEVERS, J. Pharmacol. & Exper. Therap. **51**:287 (July) 1934.

The nature of the cardiac irregularities from ephedrine and the protection from these by barbital sodium are pointed out. This is worthy of note in possible ephedrine poisoning. (The phenol barbital series is also protective in cocaine poisoning.)

PILCHER, Cleveland.

THE HOMELESS BOYS' RETREAT. JOHN LEVY, Ment. Hyg. **17**:369 (July) 1933.

On the basis of many psychiatric interviews with homeless boys passing through New York, Levy discusses the causes and results of the problem which they present. A quarter of a million adolescent boys are drifting around the country, looking for work. They travel alone, their desperate need for serving themselves first breeding a bitter selfishness. The journeys began as a healthy adolescent revolt against unfortunate home situations. The zest is gone by now, the light-heartedness and humor which are supposed to characterize the young wanderers have been replaced by suspicion, sullenness and egocentricity. Levy suggests that the personality development might have been served better by remaining at home, cheerless and hopeless as the prospect is; home, at least, would have provided congenial human contacts—the neighborhood "gang" if nothing else. Treated

leniently by authorities, devoid of any philosophic background, possessed of no class consciousness, these boys have not become socialists; each still hopes to achieve salvation through his own efforts. The personalities of the boys will probably be seriously distorted and embittered, however, and prosperity alone will never give them back their sense of humor and their well integrated personalities.

DAVIDSON, Newark, N. J. [ARCH. NEUROL. & PSYCHIAT.]

CHILD HEALTH ACTIVITIES IN A STATE DEPARTMENT OF HEALTH. E. F. WARNER, Pub. Health Rep. **49**:1056 (Sept. 7) 1934.

Some of the needs most apparent in the fields of child hygiene are improved teaching technic for nurses in the field of prenatal care, and physicians trained to render better judgment and skill in obstetric care. Child hygiene is not an entity; it should be closely bound up with the activities of rural health services. Therefore the program of a state health department ought to render the leadership, consultation, advice, method and technic for sound performance in material and child health as a part of the whole community program.

SANFORD, Chicago.

DENTAL DECAY AMONG TEXAS SCHOOL CHILDREN. JESSIE WHITACRE, Texas Agric. Exper. Stat., August 1934, p. 491.

Among 6,701 school children of Texas, dental decay was found in approximately 70 per cent of the white group, 65 per cent of the Mexicans and 45 per cent of the Negroes. The number of decayed teeth per child was greater among white children than among either Mexicans or Negroes. One or more of the 6 year molars, the first permanent teeth, were decayed in about one third of the children of each race. Among the white children, however, the 6 year molar constituted a smaller percentage of all decayed teeth than among Mexican or Negro children.

More of the younger than of the older children in San Antonio had decayed teeth, but among children in Brazos, Hidalgo and Jefferson counties decayed teeth were more often found among the older than among the younger ones. Among all the children the numbers having decayed 6 year molars increased rapidly with age up to 12 or 14 years. Slightly more girls than boys in each race had decayed teeth.

The data secured in this study suggest a beneficial effect on the teeth of liberal amounts of milk and a detrimental effect on the teeth of excessive amounts of cereals and sweet foods in comparison with other foods.

AUTHOR'S SUMMARY.

ELEVEN YEARS' WORK IN A PUBLIC SCHOOL DENTAL CLINIC. T. C. STRETTON and G. E. FRIEND, Brit. M. J. **1**:1079 (June 16) 1934.

This article is a statistical presentation of the age incidence and frequency of caries at different age periods in the different grades.

ROYSTER, University, Va.

ARE WE SATISFIED WITH THE RESULTS OF ANTE-NATAL CARE? JOHN S. FAIRBAIRN, F. J. BROWNE, ETHEL CASSIE and GEORGE F. BUCHAN, Brit. M. J. **2**:193 (Aug. 4) 1934.

This article is a symposium, with statistics and a discussion. Each author considers the subject from a different point of view of medical practice.

ROYSTER, University, Va.

HARTMANN'S SOLUTION. DE LA BROQUERIE FORTIER, Nourrisson **22**:152 (May) 1934.

Lactate Ringer's solution (prepared according to the method devised by Hartmann) was given to seven infants showing marked dehydration. In analyses of

the blood, both cells and plasma were made to show the relationship between the cell chlorides and the plasma chlorides. The normal quotient is 500. In six of the seven cases studied there was an increase in this ratio, pointing to a condition of acidosis. Following the administration of the sodium lactate solution the acidosis was usually relieved, owing to a fall in the cell chlorides; little effect was produced on the plasma chlorides. The solution had little effect on rehydration; nor did it relieve the oliguria. The urinary output was increased by the addition of Ringer's solution and sodium bicarbonate.

McCLELLAN, Cleveland.

LAZINESS IN THE SCHOOL CHILD. G. PAUL BONCOUR, Progrès méd., Sept. 8, 1934, p. 1405.

Boncour defines laziness as an attitude on account of which a school child does not make the effort necessary to accomplish the task which has been assigned to him. There may be many causes for this, and failure to analyze the lazy child may prolong further difficulties which could have been corrected. Obviously, disease conditions and endocrine disturbances should be corrected as far as is possible. Good examples and encouragement should be given. The task should not be too great for the capacity of the child, for in such a situation discouragement unfits him for what he could have done well; nor should he be allowed to do only the things which come easily to him and require no effort. The negativistic child and the child with paranoid tendencies should be recognized and given proper psychiatric attention.

LESLIE, Evanston, Ill.

STILLBIRTHS IN MEURTHE-ET-MOSELLE IN THE PAST TEN YEARS (1923-1932). A. FRUHINSHOLZ, Rev. franç. de puéricult. **2**:70 (April) 1934.

Previous to 1923 stillbirths averaged 4 per cent of all the births in this department; in the ten years 1923-1932 the average was 3.69 per cent. The improvement followed certain measures instituted in 1920-1924: in 1920, the creation of a *maison maternelle* annexed to the *Maternité* at Nancy; 1924, the organization of a departmental service of prenatal clinics; in 1922, the organization of a service at the *Maternité* for the prevention and treatment of hereditary syphilis. Since 1924 there has been little further improvement in the figures. In order to reduce stillbirths to a minimum it will be necessary to insure adequate prepartum care for every pregnant woman in the city and the country.

CRANE, Chicago.

PUBLIC EDUCATION IN CHILD CARE IN FRANCE. LOUIS DEVRAIGNE, Rev. franç. de puéricult. **2**:142 (June) 1934.

Much has been accomplished in France toward public education in child care by the establishment of clinics for the feeding of infants, prenatal clinics, antivenereal clinics and visiting nursing and medical social service. To a limited extent the schools, cinema theater and literature in the form of tracts have been used to combat ignorance. Yet to be accomplished is the program of: (1) educating girls regarding preventive medicine, (2) multiplying the number of infant clinics and of (3) prenatal clinics, (4) creating in each district a center for maternal and infant welfare, (5) utilizing to the maximum the existing laws of social assistance and social insurance for the development of national health education and (6) providing instruction in sex for school children.

CRANE, Chicago.

NATIVE ASPECTS OF THE QUESTION OF CHILD CARE IN THE COLONIES. CAZANOVE, Rev. franç. de puéricult. **2**:173 (June) 1934.

The causes of abortion, stillbirths and infant mortality in the French colonies were studied. Social causes include early marriage and polygamy. Stillbirths and deaths of infants are often attributable to rituals associated with delivery, ligature of the cord and early care and nursing of the new-born. Economic

factors affect the child in that the mother continues to do heavy work up to the time of delivery. Medical complications in the infants after birth are chiefly respiratory or gastro-intestinal. The infants go unclothed and frequently contract pneumonia. Insanitary and unsuitable foods cause frequent gastro-intestinal disturbances. The native endemic and epidemic diseases, as well as the European infectious diseases which are being introduced, take their toll of children as well as of adults.

CRANE, Chicago.

PROBLEM OF REGULAR ATTENDANCE OF INFANTS AT WELFARE STATIONS. MIGUEL A. JAUREGUY, Arch. de pediat. d. Uruguay **6**:318 (Aug.) 1934.

The author analyzes the figures for the attendance of four hundred and fifteen infants and children for a period of one year for the group under 1 year of age and for a period of eighteen months for the group aged from 1 to 3 years.

In the first group 19.6 per cent attended the clinic only once. In the second group 30.4 per cent attended only once. Among the reasons for nonattendance of the younger group were: carelessness on the part of the parents, inadequate advice at the station, the distance of the station from the home, the long wait and the promiscuous mingling of mothers in the waiting rooms. In the older group the reasons were: the greater ease in feeding and rearing children at that age, the lack of financial assistance or of free food, proximity to hospitals and carelessness on the part of the parents.

To stimulate attendance the author proposes the giving of certificates to mothers for regular attendance, coupled with donations of clothing or other objects which might please the older children particularly.

SCHLUTZ, Chicago.

DENTAL HYPOPLASIA IN THE CHILDREN OF MADRID. J. MAYORAL and J. ESCUDERO TELLECHEA, Paidoterapia **13**:361 (Aug.) 1934.

When the hypoplasia occurred in children aged from 6 months to 3 years, rickets was found to be the most frequent cause. From 3 to 6 years the most frequent cause was the eruptive fever. The prenatal and postnatal cause up to 6 months is syphilis. The authors supply proof for all these statements.

HERRON, Spokane, Wash.

PHARMACOLOGY AND PHARMACODYNAMICS OF CHILDHOOD: I. EUGEN KRAMÁR, Arch. f. Kinderh. **102**:153 (June 22) 1934.

Kramár believes that the doses of drugs generally used for infants and children are ineffective and in a great many instances not large enough. To many therapeutic agents the infant responds vastly differently than the adult. Hence the practice of calculating the infant's dose from the dose for the adult as a standard is condemned. Even in the various pediatric textbooks there is a wide divergence in the dosage recommended for infants. Up to the present time the pharmacology of drugs in infancy and childhood has not been studied from a scientific point of view. The entire question of medical dosage in pediatric practice is in need of revision.

LEMASTER, Evanston, Ill.

IMPORTANCE OF THE HEALTH RESORTS OF THE HARZ MOUNTAINS FOR CHILDREN. H. BRÜNING, München. med. Wchnschr. **81**:1052 (July 13) 1934.

Brüning urges physicians to keep in mind the Harz Mountains for the treatment of children with various subacute and chronic conditions. When the patients are under proper supervision, drink the spring waters and take the various baths they are greatly benefited. The climate, altitude and other factors vary in different parts of the Harz Mountains. For anemic, nervous or convalescent children the southern parts are better. There is some place in this mountain range which is suitable for almost any subacute or chronic condition, ranging from enlarged adenoids to tuberculosis.

BRAHDY, Mount Vernon, N. Y.

NEW METHOD OF PERCUSSION. HASSE, München. med. Wchnschr. **81**:1273 (Aug. 17) 1934.

Haase corroborates the value of the friction method for auscultation as described by Bukovala. The author has used the method for more than thirty years. He suggests another helpful point in determining the outlines of organs or in examining the lungs. If the bell of the binaural stethoscope is held in the fold between the right thumb and the hand, it is possible to percuss a finger of the left hand with the middle finger of the right hand. The sound transmitted through the finger to the rubber tubing and thence to the ears is amplified two to three times. By this method with light percussion, differences in sound, which otherwise would not be made out, can be heard. BRAHDY, Mount Vernon, N. Y.

IMPORTANCE OF CONSTITUTIONAL ENVIRONMENT IN THE TRAINING OF CHILDREN. REITER, Ztschr. f. Gesundhführ. **1**:276, 1934.

In the future all persons who are occupied with the training of children must pay attention to the problems of biology and attempt to study the limits of education set up by the inherent character of their pupils. In this way much injustice to the children will be prevented, and burdens will be lifted from educational institutions which they are incapable of carrying. REICHLE, Cleveland.

RELATIONS OF ACADEMIC ABILITIES TO SOCIAL CLASSES AND FAMILY SIZE. K. SALLER, Ztschr. f. Kinderforsch. **42**:200, 1934.

The article is a further study of the relations between intelligence, social rank and fertility. The statistics taken from the towns of Regensburg and Göttingen lead the author to conclude that the city population is decreasing in all the social classes. The actual loss in numbers is being made up by emigration from the country where, however, the decrease in the size of the family has also assumed proportions which will lead to a decrease in the total population. Although these changes are seen in all the social classes, the decrease is by far the greatest in the higher ones and becomes less marked as one proceeds downward. It is particularly important that there is a considerable difference between the fertility in the families of special classes and in those of the untrained laborers.

REICHLE, Cleveland.

DEVELOPMENT OF INSTITUTIONAL CHILDREN IN THE FIRST YEAR. H. DURFEE and K. WOLF, Ztschr. f. Kinderforsch. **42**:273, 1934.

The authors call attention to the fact that although the mortality of infants in institutions has now been decreased to such an extent that in the better institutions the rate is no higher than the general death rate, yet the problem of the mental development of these children is still acute. Examination of many institutions in Germany has lead them to conclude that the monotony, the excessive bodily hygiene and the lack of color and personal stimulation found in almost all institutions lead to a lag in the mental development of infants who are kept in these institutions. They point to the fact that the presence of mothers in institutions taking care of infants greatly improves the results, but that this depends entirely on the amount of interest which the mother has in the child. They suggest certain improvements in institutions for infants which they do not regard as unpractical and which are designed to lead to greater variety in the daily life of the child.

REICHLE, Cleveland.

RELATION OF ABNORMAL CHILDREN IN THE TOWNS OF REGENSBURG AND GÖTTINGEN TO THE SOCIAL STRUCTURE OF THE ENTIRE POPULATION. K. SALLER, Ztschr. f. Kinderforsch. **42**:447, 1934.

Saller has found that the abnormal children in special classes of these cities come primarily from the lower social classes. This is true not only for the parents

but also for the grandparents. In other words, this class shows a pronounced tendency to deteriorate socially. This is chiefly due to the heredity and in part also to the environmental conditions.

REICHLE, Cleveland.

STUDIES ON TWINS IN INFANCY AND PRESCHOOL AGE PERIODS. LUISE BRAUNS, Ztschr. f. Kinderforsch. **43**:86 (July) 1934.

Brauns believes that she has proved that the method of Siemens and von Verschuer may be applied to children in the preschool age period and that it is possible to distinguish between monozygotic and dizygotic twins accurately and readily. Nevertheless, she discusses three cases of twins among the one hundred and sixty pairs which she examined which she regards as instances of borderline twins. Furthermore, in her discussion she points out that many of the characteristics used in the scheme of diagnosis, such as the color of the eyes, hair and skin, undergo changes in the course of growth. She does not, however, apparently believe that these indeterminate factors influence adversely the method of diagnosis. Practically no attention is given to the publications of other authors who have not been able to substantiate the claims of von Verschuer. In particular, finger-prints and palm-prints, the unreliability of which has been repeatedly shown in the past, are still used by the author, although no information is given as to how the discrepancies discovered by previous workers could be avoided.

REICHLE, Cleveland.

Society Transactions

CHICAGO PEDIATRIC SOCIETY

Clinical Meeting, Sarah Morris Hospital, Oct. 15, 1935

JESSE R. GERSTLEY, M.D., *Presiding*

LETTERER-SIWE'S DISEASE. DR. EDWARD DENENHOLZ.

This boy, aged 2 years, was brought to the hospital because of a gradually increasing swelling over the left side of the head, of six weeks' duration. There was a nevus over the frontal area, which had been treated with carbon dioxide snow one year before entrance. The most conspicuous feature was the pulsating mass with a loud bruit over the frontal area. The spleen could be felt; the liver was just palpable, and there were a few small lymph nodes. The differential blood count was normal. When a lateral roentgenogram of the skull was made a large defect in the bone underlying the pulsating mass was revealed. Roentgenographic examination of the long bones gave negative results.

The course in the hospital was down-hill. The mass on the head gradually increased in size. The temperature reached from 101 to 104 F., and the anemia and leukopenia increased. The patient was given radium therapy and blood transfusions but expired three months after admission.

Because of the mass on the head and the nevus over the frontal area it was believed that the condition was a malignant form of hemangioma. Later, because of the defect in the skull with the leukopenia and anemia, the diagnosis of Schüller-Christian's syndrome was ventured. Then, as enlargement of the liver, spleen and lymph nodes persisted and the anemia increased, it was thought that the condition most closely resembled clinically aleukemic leukemia.

Microscopic examination revealed marked infiltration and hyperplasia of large, pale nonlipoid-storing macrophages, histiocytes and reticulo-endothelial cells in the various internal organs and the mass on the head. Dr. Arthur Abt and I reviewed the literature and found records of several cases; the first was reported by Letterer in 1924 and later by Siwe in 1933. The disorder is neither familial nor hereditary. It occurs in infants and young children, the oldest patient reported on being 2½ years old. The course is progressively down-hill, and death occurs within from a few months to two years. Generalized lymphadenopathy is present. The patients reported on showed typical pathologic changes in the lymph nodes, but thus far biopsy has never been performed. Petechiae are apparent, and osseous changes are frequent but may be recognized only by roentgen examination or at autopsy. Examination of the blood shows only anemia, with a normal differential cell count. Most cases are reported under the term reticulo-endotheliosis, although under this term are included a wide variety of illnesses of heterogenous etiology. This disease is of unknown etiology, and my associates and I believe, along with Siwe, that it is a clinicopathologic entity.

TETANY OF THE NEW-BORN, WITH DEPOSIT OF CALCIUM FOLLOWING PARENTERAL ADMINISTRATION. DR. I. HARRISON TUMPEER.

A new-born premature infant was sent to the pediatric ward with the diagnosis of cerebral hemorrhage and bronchopneumonia. The condition was readily determined to be tetany of the new-born; this was confirmed by determinations of the blood calcium and reactions to the galvanic current. Preparations of calcium were given intramuscularly in the buttocks, together with parathyroid extract. Improvement was noted in the baby's general condition, but in the fourth week a bony hard induration of the buttock and part of the thigh became manifest. Roentgenograms

demonstrated an irregular deposit of calcium along the fascial planes from the hip to the knee. A small mass sloughed through and proved to be calcium phosphate on chemical analysis. The extensive deposit of calcium was gradually absorbed, so that little remained when the child was discharged from the hospital at the age of 4 months.

Incidentally, the child is now over a year old and in good physical condition, but teeth have not yet erupted.

In addition to being another case of typical tetany of the new-born with many other clinical manifestations omitted in this brief abstract, this is the first case reported in which there was objective evidence that the disturbed calcium metabolism in tetany is expressed by disturbance in absorption.

NITROBENZENE POISONING IN INFANCY. DR. LOUIS S. ROBINS.

In November 1934, a 2 month old baby was brought into Sarah Morris Hospital with a history that it was well until the morning of admission, when the mother noticed that the baby was blue all over. On examination the cyanosis was the only finding of note. The temperature, blood and urine were normal. When the mother was questioned more closely it was learned that bedbugs had been found in the room. She had obtained liquid insecticide from the house management and sprayed it in the room and on the crib the afternoon before admission and had put the baby in the crib that evening. A sample of the insecticide was analyzed and was found to contain nitrobenzene. Examination of the blood for methemoglobin gave negative results. The infant was put in an oxygen tent over night, and the next day a transfusion of 60 cc. of blood was given. The cyanosis subsided two days later.

Three weeks later another child who lived in the same building was brought in, with the same history of being well until that morning, when the parents noticed that it looked blue. The child did not cry, and they did not bother about it. Another child in the family was ill, and while the doctor was there to see this patient he was asked to look at the blue baby. He advised that the child be taken to the hospital immediately, and it was brought in at 8:00 p. m. Remembering the case of a few weeks previously, my associates and I asked about bedbugs and were told that there were none in the apartment, but questioning revealed that an old baby-buggy had been presented to the family the day before and was found filled with bedbugs. The mother sprayed the buggy about 11 o'clock in the morning with the same insecticide that was used in the first case, aired the buggy for several hours and then put the child to sleep in it. In the morning the child was cyanotic. That child also was given a transfusion and put in an oxygen tent. The next morning the cyanosis was the same. We then removed 1½ ounces (42.5 Gm.) of blood from the sinus and injected 2½ ounces (70.9 Gm.) of blood into the vein. Within a few days the child was sent home.

The important points learned from these cases were that a sudden onset of unusual cyanosis out of proportion to other symptoms should suggest nitrobenzene poisoning, which prevents absorption of oxygen. It should also be remembered that the poisoning takes place in most cases by absorption through the skin and not by inhalation. The literature contains numerous reports on infants with poisoning from nitrobenzene absorbed from diapers freshly stamped with ink. Our patients did well on treatment with oxygen and blood transfusion, though some authors reported cases in which the patient recovered without any treatment.

ENCEPHALITIS FOLLOWING GERMAN MEASLES. DR. ABRAHAM LEVINSON.

Encephalitis following vaccinia, varicella, mumps, pertussis and measles has been known for a good many years. There is, however, little in the literature in regard to encephalitis following German measles. Only two articles on the subject appeared previous to 1935, and those were in the French language. Two reports have appeared in this country this year.

During the last year I have seen two patients with encephalitis following German measles. The first patient was a girl, aged 8 years, who was well until May 27, 1935, when a papular rash on the face and posterior cervical adenitis developed. The rash spread over the neck and by the following day involved the entire body and became blotchy. There was little or no fever. There was no question of the diagnosis of rubella. Two days later the rash began to disappear, but the child did not eat well on that day and by evening became nauseated and vomited; she cried all night. The nausea and vomiting continued for two days. On the fourth day following the appearance of the rash the temperature was 102.6 F., and the patient started to talk irrationally. On the fifth day she seemed brighter for a while, but later in the day became lethargic, had repeated convulsions and sank into a deep coma.

There was a history of scarlet fever six months previously, chickenpox a year previously and measles three years previous to the German measles. The tonsils and adenoids were removed at 2½ years of age. She was vaccinated at the age of 3 years. Otherwise, the previous history and the family history were unimportant.

She was brought to the hospital on May 31 in a state of coma, with repeated general convulsions and a temperature of 103.8 F. The pupils were dilated and reacted to light sluggishly. There was some inequality of the face. The reflexes were not exaggerated. The next day the coma was not as deep as the day previously, but she had signs of meningeal irritation. She continued to show improvement and on June 6 she yawned a great deal, opened her eyes and responded to some questions.

The next day she was still more responsive and sat up in bed. From that day on she continued to show improvement, except for a residual halting of speech, which improved, and conjunctival injection, which improved gradually. The temperature, which was 103.8 F. on admission to the hospital, rose to 105 F. on June 1, but came down gradually, and on the fourth day it was normal and stayed down.

On admission the red cell count was 3,940,000, with 70 per cent hemoglobin. Leukocytes numbered 14,950, with 71 polymorphonuclears, 21 lymphocytes, 7 monocytes and 1 eosinophil. On June 10, the white cell count was down to 4,900, with 46 neutrophils, 50 lymphocytes and 4 monocytes. The urine was normal throughout the course.

The cerebrospinal fluid obtained by spinal puncture on the day of admission was increased in amount and in pressure. The cell count was 160, with 60 per cent polymorphonuclears and 40 per cent lymphocytes. The Pandy reaction was 4 +; the Ross-Jones reaction, 2 +. The sugar content was 88 mg. per hundred cubic centimeters. The blood sugar content was 104 mg. per hundred cubic centimeters.

The treatment consisted in spinal puncture, which was done on two occasions, the administration of fluid subcutaneously and sedatives when indicated.

The second patient behaved practically the same as the first. Encephalitic symptoms set in on the fourth day following the appearance of the rash of German measles in a 6 year old boy, with a temperature of 101 F. and convulsions. The cerebrospinal fluid was clear and contained 35 lymphocytes; and the globulin tests gave positive results. The cerebrospinal fluid pressure was not increased, and the sugar content was 91 mg. per hundred cubic centimeters. The next day hemiplegia developed on the right. All the symptoms subsided gradually. These 2 cases show that encephalitis following German measles is not rare and should be taken into consideration whenever acute neurologic manifestations occur following this disorder.

ALLERGY DUE TO MENOTOXIN. DR. MEYER A. PERLSTEIN.

One hesitates to report a case of allergy due to human emanations, not only because the condition is so rare and to date experimentally unattainable but also because of the fact so recently emphasized by Vaughn in the *Journal of the*

American Medical Association that allergy due to cohabitation is usually traceable to substances other than human emanations about the offending person.

This 6 year old colored girl was brought to the clinic in February 1934, with the story that for the previous ten months she had suffered a severe attack of bronchial asthma on about the fourteenth day of each month. These major attacks were interspersed with fortnightly minor attacks of asthma. There was no history of any offending substance, and the only history relative to allergy was that an uncle on the maternal side had had asthma.

However, the following interesting correlative history of the mother was obtained: Ten months previously she had become pregnant, and on the fourteenth of each month thereafter, instead of having a menstrual period she had profuse leukorrhea which lasted from five to seven days. At the same time the child, who slept with her mother, had a severe attack of asthma. There was no history of the fact that the mother used any douche or deodorant during these periods that was not used at other times.

The mother gave birth to a child on Dec. 14, 1933, and on this night the patient experienced her worst attack of asthma. The mother nursed her infant and up to the time of admission to the clinic, in her third puerperal month, had continued to have monthly leukorrheal periods, which were accompanied by attacks of bronchial asthma in the patient.

Complete skin testing revealed that the child was sensitive to ragweed, house dust and three vegetables. Weekly desensitizing doses of the two former were given and the offending foods removed from the diet. Skin tests done with various ovarian preparations, antuitrin S, solution of pituitary and other preparations caused no wheal formation. A speculum specimen of the maternal leukorrheal secretion was obtained, and extracts were made from this, as well as from Kotex pads used before, during and after her period and from an unused Kotex pad. In addition, vaccines and filtrates were made from the organisms cultured from the leukorrheal secretion. Skin tests done with these revealed the child to be sensitive to only one substance, namely, the leukorrheal extract. Repeated tests with this substance caused a marked wheal with pseudopod formation, while the other extracts caused no such reaction.

The mother was then instructed to have the patient sleep alone during her next period, with the result that for the first time in eleven months the child missed her attack of asthma. The next month the child was allowed to sleep with her mother and again had an attack of bronchial asthma. Since then the child has slept alone and has been free from monthly attacks associated with the maternal period. She still has occasional sporadic attacks, usually following an infection of the upper respiratory tract.

It is also of interest to note that about four months after coming to the clinic, in her mother's seventh puerperal month, the child failed to react positively to the leukorrheal extract to which she had previously reacted positively. Passive transfer also failed. Whether or not this indicates that freedom from an antigen may cause desensitization to it I cannot state.

MALIGNANT THYMOMA. DR. JOSEPH GREENGARD.

A boy, aged 5 years, was admitted to the hospital in June 1932, with the complaint that a mass over the upper portion of the sternum and a similar mass behind the left ear had been present for five months. In addition he had had polyuria and polydypsia for two years. The mother stated that the child was struck with a toy wagon over the chest and behind the left ear, following which he bled from the nose and mouth. Shortly after this the nodules appeared over the involved areas and gradually increased in size until on admission there was a fungating mass over the chest and behind the left ear, as shown in the photograph. Roentgen examination revealed diffuse infiltrative lesions involving both pulmonary fields, which were considered metastases. A lateral view of the chest when the child was admitted showed a destructive lesion involving the second sternal segment. The

roentgenogram of the skull showed erosion of the left mastoid process. This was also considered to be a metastatic malignant lesion by the roentgen department.

The child was treated with radium in the clinic for patients with tumor, with a brilliant result. [Roentgenograms were presented.] He is now perfectly well, both tumor masses having healed completely. There is no tenderness. There are still some physical signs over the lung, and the symptoms of diabetes insipidus persist to some extent.

A biopsy was performed on the lesion when the child was admitted; this showed microscopically two different types of pathologic change. There were considerable infiltration by inflammatory cells of various types, nonspecific granuloma and, in addition, specific, large ovoid tumor cells showing numerous mitotic figures with a well developed reticulum. In view of the character of the histologic changes and the location of the principal mass, the lesion was considered to be a malignant tumor originating in the thymus gland, a thymoma. Since the origin of the cells of the thymus gland embryologically is not well defined, one cannot be certain whether these tumors are carcinomas or sarcomas. Ewing, therefore, states that it is best to call them malignant thymomas without any more definite attempt at classification.

As to the relationship of the injury to the development of the lesions, the two areas were the ones that the mother said were struck by the toy wagon. The coincidence of diabetes insipidus, which has been attributed to lesions of the pituitary gland, is of interest in this instance of a tumor involving the thymus gland. The therapeutic result has been very satisfactory, with complete absence of symptoms for a little more than three years.

LESIONS OF THE URINARY TRACT IN CHILDREN. DR. ALFRED E. JONES (by invitation).

I wish to show some patients illustrating the value of the intravenous pyelogram. Physicians have been cautioned against treating infections of the upper urinary tract over a prolonged period without urologic investigation. Now we have the intravenous pyelogram for diagnostic purposes, which is invaluable and has almost entirely supplanted other methods.

CASE 1.—A girl, aged 9, had pain in the upper left quadrant of the abdomen for six years. It was not very severe but annoying. She was taken from one physician to another, without any satisfaction as to diagnosis or treatment. Urinalysis gave normal findings. An intravenous pyelogram revealed a double ureter with a double pelvis, the lower much smaller than the upper, and my associates and I explained that this was probably the cause of the pain. We did not recommend any treatment because the kidney was not infected, but we told the parents that if it ever became infected or the pain became severe we might have to think of surgical intervention.

CASE 2.—A 6 month old boy was treated for pyelitis for four months. When the urine became thick with pus and chills and fever developed the child was brought to the hospital. The intern administered an intravenous injection of skiodan, which showed, instead of the usual clover-leaf formation, three large cavities revealing complete destruction of the right kidney. As the other kidney was normal, we removed the infected one. I think that this is the youngest patient on record on whom nephrectomy was successfully performed for whom the diagnosis was made before operation. The patient is now about 5 years old and is perfectly well.

CASE 3.—This case is one of a congenital anomaly of the lower urinary tract. This boy was born without a urethra, with an opening resembling a suprapubic cystostomy fistula. He is now 9 years old and was first seen at the age of 6 years. He had to wear a napkin all the time, which was constantly soaked with urine, and he could not be taken to school. We transplanted the ureters into the sigmoid flexure, according to the first operation described by Coffey. The child got perfect control and was able to void at will. During the first few months

following operation he had attacks that were thought to be attacks of pyelitis. The temperature rose, and there was marked pain, but the symptoms disappeared after an enema was given. The boy now goes to school and plays like normal boys. He gets up perhaps once during the night but has no trouble. We attempted to make a urethra for him but succeeded only in part. We brought the opening above the symphysis part way down and shall try again later to get it down farther.

COARCTATION OF THE AORTA. DR. SIMON A. WILE.

Clinical recognition of coarctation of the aorta is rare during childhood. This patient has stenosis of the aortic isthmus, with all the associated signs. She is now 15 years old and was first seen at the age of 2 years, at which time physical examination gave negative results except for a mottled appearance of the skin over the arms and a roughening of the first heart sound at the apex. At 6 years of age she was admitted to the hospital with acute rheumatic fever and endocarditis. At the age of 7 she was readmitted with acute chorea. When seen in the clinic for cardiac disease after her discharge it was found that she had marked hypertension. In an attempt to explain this hypertension the blood pressure was taken in the legs and found to be normal. This finding, together with a systolic murmur over the precordium, enlargement of the left ventricle and the mottling of the skin over the arms and shoulders, raised the question of the presence of coarctation of the aorta. During the past several years the girl has been well. Apparently the only subjective symptom has been a lowered tolerance for exercise.

Physical examination at present reveals a well nourished and well developed child. There is a noticeable pulsation in the neck, with a thrill in the suprasternal arch. One can note the mottled, cyanotic appearance of the skin over the arms and shoulders. The heart measures 8.5 by 3.5 cm. There is a rough systolic murmur over the precordium, which is loudest at the third left interspace. The electrocardiogram is normal. A roentgenogram of the chest shows enlargement of the heart, particularly of the left ventricle. There is, however, an absence of the large aortic knob usually associated with hypertension. The inferior borders of the ribs show the characteristic scalloped appearance.

This condition is an example of the adult type of coarctation of the aorta. Children with the adult type of coarctation live for some time, but most do not live as long as this patient. Death usually results from intercurrent infection, failing circulation or rupture of the heart or aorta.

ANGIOSARCOMA OF THE FEMUR IN A NEW-BORN INFANT. DR. JULIUS H. HESS.

My associates and I are not certain whether this tumor was primary or secondary in the femur. The child is now 4 months old and at birth had marked enlargement of the lower part of the right thigh, involving the knee joint. The patient is now well nourished and seems to be in good condition, except for the tumor mass. At birth it was impossible to make extension or flexion of the right knee, owing to a bulging, fluctuating mass in the popliteal space. On the second day of life a roentgenogram was made of the right femur, which showed marked erosion of the shaft of the femur in the lower third. The infant was brought to the hospital at the age of about 18 days, and a roentgenogram at that time showed the bone destruction still present. We thought of the possibility of an intra-uterine gumma, a cystic hygroma or a malignant tumor. We punctured the popliteal space and obtained 15 cc. of serosanguineous fluid, which on culture proved normal. The blood and urine also were normal.

The child was taken to the roentgen department for treatment and was given 1,200 roentgens in split doses, 300 each day for four successive days. She was kept in the hospital for about three weeks and was then sent home and returned four weeks later for another series of treatments. She has now returned for a third course. Roentgenographic examination shows that the bone is beginning

to fill in, and the central canal is well developed. The leg is still large but is somewhat smaller than it was in August. A roentgenogram of the chest showed no metastasis.

We punctured the soft tissues of the tumor with a large-caliber needle. Small masses of tissue removed in this way were reported as being angiosarcoma.

Notwithstanding the local improvement and the progress that the infant has made, the prognosis remains uncertain.

NEUROBLASTOMA IN AN INFANT. DR. JOSEPH K. CALVIN.

This infant, now 6 months of age, has been under observation for two months. There were no particular symptoms. The child eats fairly well, seems happy, gains weight slowly and has no fever, but on palpation a markedly enlarged liver was discovered. It is firm, irregular, nodular and apparently not tender. There is no apparent enlargement of the spleen, and there has been no jaundice or ascites. An intravenous pyelogram showed normal renal calices and no displacement or distortion of the size, position or shape of the kidneys. No metastases were seen in roentgenograms of the bones and chest. At exploratory laparotomy the liver was markedly enlarged, firm and studded with nodules up to 1 cm. in diameter, which were grayish-yellow, hard and avascular. The adrenals and kidneys felt normal on palpation. Biopsy of the nodules in the liver revealed what at first glance microscopically appeared to be a small round-cell sarcoma consisting of cells of various sizes, shapes and staining properties and occasional mitotic figures. However, on closer examination the cells showed a tendency to arrange themselves in rosettes, characteristic of blastoma. Another section was stained with a special silver stain which brought out the nerve fibers, and then it was apparent that the small round cells that seemed to be sarcoma were really stellate-appearing embryonic ganglion cells with axons and dendrites, a typical neuroblastoma metastatic in the liver. The site of the primary tumor is as yet undiscovered. Usually it is the adrenal (Pepper type) or the sympathetic prevertebral ganglions along the aorta.

This type of tumor does not respond to irradiation, so there has been no treatment in this case, but the liver seems to be definitely receding in size, and the child's general condition is improving, at least temporarily, although this type of tumor is supposed to be very malignant, with a rapid down-hill course. There are as yet no demonstrable metastases in the bones or lungs.

ARACHNODACTYLIA. DR. ALWIN C. RAMBAR.

C. N., a Negro boy, aged 28 months, was first seen at birth. He was a premature infant, weighing 1,815 Gm. at birth, with a length of 44.5 cm. At that time it was noted that he had abnormally long fingers and toes and that his ears were unusually large. At the age of 2 months bloody snuffles and cracked and scaling palms and soles developed, and he had a 4 + Wassermann and Kahn reaction. He was treated with acetarsone, and after one course of treatment the serologic reactions were reversed. He was not seen from 6 months until 2 years of age, when he presented the following findings: His face is long and aged; the supra-orbital ridges are prominent; the ears are extremely large. The hands and fingers are long and slender, as are the arms, legs, feet and toes. There is hypermotility of the joints, especially the wrists and ankles. The feet are in equinovarus. The body musculature is poor, and there is generalized absence of subcutaneous fat. He can walk only by holding on to stationary objects. He has marked kyphosis, with scoliosis and a pigeon breast. His body length is 45 inches (114.3 cm.), and his span is 45½ inches (115.6 cm.), 5 inches (12.7 cm.) more than normal for his age. He is subnormal mentally. His eyes show the characterisitc findings of this disease, namely, megalocornea, extreme miosis, resistance to dilatation with atropine and subluxation of the crystalline lens. This disease, arachnodactylia, was first described by Marfan in 1896 and is known as

Marfan's disease. Practically all the characteristics described are shown by this patient. About 75 cases have been reported. The disease is congenital and often familial and is possibly due to some type of pituitary involvement.

ANTHOCYANINURIA. DR. ABE MATHESON.

Anthocyanin is a pigment abundantly present in red beets. Although this food is a common article of diet in children, the presence of this pigment in the urine is rare. When it does occur it discolors the urine a light to a dark red, depending on the concentration of the pigment. In such instances it may be difficult to distinguish such a specimen from one of a patient with hematuria. The chemical characteristic of this pigment is such that on the addition of alkali the color changes to yellow, after which the addition of acid restores its original color.

My attention was called to this when I was asked to see a boy, aged 4 years, who, as the mother stated, had been passing bright red blood in the urine and was to be hospitalized for diagnosis. The child was not ill. There was no history of infection, trauma or the intake of drugs. The specimen of urine presented to me appeared to be one of a person with hematuria. Tests for blood, cells and albumin gave negative results. Such a condition following the ingestion of red beets was described in the May 1927 issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN. The mother was then questioned about the diet and voluntarily informed me that the child had been eating many red beets. When they were discontinued the urine cleared in a short time.

I present this instance to illustrate a point in the differential diagnosis of red urine.

HEMORRHAGE IN THE COURSE OF RETROPHARYNGEAL ABSCESS. DR. SAMUEL J. PEARLMAN (by invitation).

The figures and cases used in this discussion tonight are part of a more extensive study made by Dr. Samuel Salinger and myself and intended to determine the incidence, pathogenesis, pathologic features and treatment of severe hemorrhages occurring secondary to infections about the pharynx. While the number of cases gleaned from the literature would make hemorrhage occurring in the course of retropharyngeal abscess appear to be uncommon, it is probably true that most cases are not reported and that nearly every pediatrician in the course of a lifetime of practice observes one or more such cases.

How do these hemorrhages come about? In the first place, they are not hard to understand if one remembers that retropharyngeal abscess occurs over the entire length of the pharynx, from the roof of the skull to the level of the larynx. Hence they are in close proximity to the internal carotid or common carotid arteries, less often other vessels. The mechanism of the hemorrhage is about as follows: The wall of the common or internal carotid artery is bathed in pus and becomes weakened. Finally either it ruptures directly or it bulges to form a false aneurysm which eventually ruptures. Bleeding occurs then from the pharynx or nose, or, if the false aneurysm burrows deeply enough, bleeding takes place via the ear and is hence very deceptive, and its true significance is not truly appreciated.

Why in some instances of retropharyngeal abscesses is there hemorrhage, and why is it absent in a large majority of cases? This is not known, except that hemorrhage is possibly due to a number of fortuitous circumstances: (1) the size of the abscess and its duration and location; (2) the nature of the organism producing the infection; (3) the fact that the normal internal carotid artery makes a number of distinct curves in its course from the neck to the skull and that an unusually full curve in some persons brings it close to the area usually involved in retropharyngeal suppuration.

The hemorrhage may occur as one of a number of types:

(1) Sudden foudroyant bleeding, with death at once. There is little or no protection against this calamity.

(2) Several severe hemorrhages. These at least give some warning.

(3) A number of apparently minor hemorrhages followed by a severe fatal one.

Treatment is ligation of the common carotid artery on the affected side. Of course, ligation of the common carotid artery has some risks. A review of the world's literature for the past hundred years shows that at all ages, from early youth to age, the dreaded serious intracranial complications after ligation occur in about 25 per cent of the cases, and in these there is a mortality of about from 10 to 15 per cent. On the other hand, in our series of 32 retropharyngeal abscesses which bled, ligation was not performed in 25 cases, and all but 1 patient died—a mortality of 96 per cent. The common carotid artery was ligated in 5 cases, and 3 patients recovered. In another group of 25 cases of retropharyngeal abscess complicated by involvement of the parapharyngeal space in 13 patients ligation of the common carotid artery was not done, and all the patients died. In 14 cases the common carotid artery was tied, and 8 patients recovered. Hence, the chances of any single patient for recovery are much greater after ligation of the common carotid artery. This is made especially clear if one reflects that in 31 cases of this kind in which the patient came to autopsy, the arteries involved 26 times were either the common or the internal carotid arteries.

Hydranencephaly (Cruveilhier). Dr. Ethel M. Davis.

B. H., an infant born spontaneously by breech delivery after twenty-seven weeks' gestation, weighing 1,300 Gm., was cyanotic when brought to the station for premature infants and was placed in an oxygen incubator. The child was very feeble, crying at times; it was fed by gavage and died on the sixth day. The spinal fluid was xanthochromic, and a diagnosis of intracranial hemorrhage was made.

On section the head was rather larger than normal. When the skull was opened about 200 cc. of clear yellow fluid was present, the brain occupying only the base of the skull. The ventricles and the aqueduct of Sylvius were wide open, the choroid plexuses being exposed; the frontal portion of the cerebral hemispheres was absent, the occipitoparietal lobes being rudimentary and the medulla and cerebellum very small.

This condition, which was first described by Cruveilhier in 1792, is characterized by a rudimentary cerebrum and a cranium of normal size.

Tuberous Sclerosis. Dr. Ethel M. Davis.

J. W., aged 2 months, was brought to the hospital with symptoms of basal meningitis: vomiting, opisthotonus, conjugate deviation of the eyes and bulging of the widely open anterior fontanel. Spinal puncture yielded a normal fluid. The diagnosis of tumor of the brain was made, but operation was not advised.

On section the architecture of the base of the brain was obscured by yellowish-white masses of firm tissue, which also invaded the cerebellum and medulla. The ventricles were dilated, and on the floor of the fourth ventricle was a similar tumor mass. The right trochlear nerve and both oculomotor nerves were absent.

Microscopic sections of the nodular masses at the base of the brain revealed a marked new formation of glia fibers and nuclei (cresyl violet stain). Masses of cells with oval vesicular nuclei invaded and replaced the brain tissue. In some instances the nuclei surrounded the perivascular spaces in the form of pseudo-rosettes (unipolar spongioblastomas).

This condition is similar to that described as tuberous sclerosis associated with sebaceous adenoma and neurofibroma of the skin and renal cortex. Clinically, the triad of mental deficiency, sebaceous adenoma and epileptiform seizures has been described under the name of epiloia (Lind).

Foreign Bodies in the Urogenital Tract. Dr. Philip Rosenblum.

Children put foreign bodies in the vagina and urethra with sufficient frequency that they must be considered in all differential diagnoses of urogenital conditions.

The first patient is a girl who had been under treatment for several months for so-called chronic pyelocystitis. When I first saw her she had considerable pus in the urine, with some bright red blood at times and marked dysuria. Examination showed slight elevation of the temperature and secondary anemia, but on fluoroscopic examination one could see a stone in the bladder, and the roentgenogram showed a pin inside the stone. The pin was a so-called "tailor's pin" with a T-shaped head. The child was admitted to the hospital. A cystostomy was performed, and the stone and pin were removed. The wound healed promptly after removal of the tube, which was left in four days, and all the symptoms subsided.

The second girl, aged 10 years, was admitted to the hospital with the diagnosis of hemorrhagic nephritis because of the presence of blood in the urine for three months. The physical findings were not compatible with that diagnosis. A roentgenogram was made which revealed a hairpin in the bladder, but it did not show the stone in which the pin was embedded. The patient was rather large, and the urologist removed the stone and pin through the urethra. The removal was readily accomplished by crushing the stone and bending the pin.

The third patient is a girl, aged 4½ years, who was seen because of a slight bloody discharge from the vagina for two or three weeks. Under fluoroscopic examination a foreign body could be seen in the vagina, and it was easily removed with forceps. This proved to be a metal screw from the bathtub.

The fourth girl, aged 5 years, had been treated for several months. A diagnosis of precocious menstruation had been made. She did not object to my examination, an observation which I have made in children who masturbate. Too much modesty, as well as insufficient modesty, should make one suspicious. I placed an applicator in the vagina, being careful to see that the cotton was wrapped on it carefully, and it came out discolored black. In this case a marble, a button and a penny were removed. The bleeding was due not to the presence of the foreign bodies but to the fact that the child while in bed had tried to remove these objects with scissors.

The principal symptoms of a foreign body in the bladder are dysuria and hematuria, while unexplained bleeding from the vagina should always lead one to suspect the presence of a foreign body.

ERYTHEMA ANNULARE RHEUMATICUM. DR. ARTHUR F. ABT.

In 1922, Lehndorff and Leiner, under the title "Erythema Annulare" published an account of a typical exanthem occurring during the course of rheumatic endocarditis. Lehndorff, in 1930, again described "erythema annulare rheumaticum" and emphasized the fact that it occurs only in rheumatic children with endocardial involvement. While making the rounds at the Mautner-Markhof Kinderspital in Vienna in 1925, the late Professor Leiner demonstrated this rash to me in a child with rheumatic endocarditis. I have had the opportunity to follow a group of children suffering from rheumatic endocarditis at the Spaulding School for Crippled Children, and during the course of my examinations I have noted this distinctive rash in 6 children.

Erythema annulare rheumaticum (Lehndorff-Leiner) is a specific exanthem associated only with rheumatic endocarditis. The lesions are pale red or bluish red semicircles or rings which on first appearance may be from 2 to 4 mm. in diameter and which may develop into rings of from 1 to 3 cm. in diameter. The lesions are found on the chest, over the abdomen, on the sides of the thorax and on the back. They are rarely seen on the extremities and never on the face or mucous membranes. The lesions are never papular but always macular. There is no itching, edema or hemorrhage associated with them. They disappear without scaling or pigmentation.

Lehndorff estimated that erythema annulare rheumaticum occurs in about two thirds of all cases of rheumatic endocarditis in children. Because of its transitory nature it is probably overlooked. The rash is not associated with septic or ulcerative endocarditis or endocarditis lenta and does not occur in other types of arthritis.

Its prognostic value, in my experience, is varied. In the 1 fatal case in which it occurred it was an ominous sign. In the other 5 children the rash has been noted after illnesses varying from slight colds without febrile reaction to recurrent attacks of rheumatism with fever.

Arvid Wallgren has recently observed erythema annulare rheumaticum in 12 per cent of the patients with acute rheumatic endocarditis in his hospital. He believes that the erythema may be regarded as an angioneurosis arising on a rheumatic allergic basis.

If one examines Cheadle's classic monograph "The Various Manifestations of the Rheumatic State" (1889), one notes as a frontispiece a colored print sketched from life, depicting a posterior view of the head and back of a child, showing large subcutaneous nodules on the occipital region of the head, along the spine, over the wings of the scapulae and over the posterior iliac crests. Besides these nodules, one notes annular cutaneous lesions which in the picture appear similar to erythema annulare rheumaticum and which Cheadle termed erythema marginatum. The following statement from Cheadle's work agrees with the precepts of Lehndorff and Leiner: "These varieties [referring to the cutaneous lesions mentioned] are not infrequently associated with endocarditis and pericarditis in the most serious cases."

THE MEDICAL TREATMENT OF UNDESCENDED TESTES. DR. RALPH H. KUNSTADTER.

In 1932, Engle produced experimental descent and growth of the testes and growth of the scrotum in immature macacus monkeys by injections of anterior pituitary-like hormone extracted from the urine of pregnancy.

Following Engle's report, Dr. Louis Robins and I treated 8 boys with a condition classified as juvenile hypopituitarism of the Fröhlich type with a commercial extract of the urine of pregnant women. We found that descent of the testes resulted in the 3 cryptorchids of this group. Since we reported this study in 1933, 25 patients in all with juvenile hypopituitarism have been treated. All the boys presented hypoplastic gonads, and 10 had either bilateral or unilateral cryptorchidism. In 9 the cryptorchidism was bilateral and in 1 unilateral. For this presentation I am showing the results of treatment of the 10 boys with endocrine cryptorchidism and of 3 with nonendocrine cryptorchidism. This work is presented chiefly for two reasons: first, because of the skepticism of many as to the value of medical treatment of undescended testes and, second, because of the desire of my associates and myself to follow these patients and determine whether there were any untoward reactions or precocious development.

Treatment consisted of the hypodermic administration of anterior pituitary-like hormone in doses of from 100 to 150 rat units given three times weekly over a period of from three to six months. The most satisfactory results are obtained at the preadolescent and adolescent ages. Satisfactory results were obtained in all the cases of endocrine cryptorchidism. Descent and growth of the testes and growth of the scrotum, with the appearance of secondary sex characteristics, occurred in many of the patients. There were no untoward reactions in any of our cases, and in no instance was precociousness observed. The 3 boys with nonendocrine cryptorchidism, 2 of whom had unilateral cryptorchidism and 1 bilateral cryptorchidism, failed to respond to treatment. Unquestionably, a mechanical factor was present, preventing descent of the testes.

The question frequently arises why not wait for self-regulation of the endocrine condition and spontaneous descent of the testes? There are several factors against this argument. Cooper has shown that retrogressive changes occur in the testes of cryptorchids after from 2½ to 3 years of age. There is also the possibility that a testis that is already atrophic may become more atrophic. The cosmetic and psychic effect on the patient must be considered. In private practice parents request that something be done for this condition.

In summary, it may be stated that in cryptorchidism associated with endocrine dysfunction treatment with anterior pituitary-like hormone is indicated. In the

patients with nonendocrine cryptorchidism, usually unilateral, with normal growth and development of the remaining testis, a mechanical factor is most often present, and treatment with anterior pituitary-like hormone is of questionable value. A definite distinction should be made between these two types. As an adjunct to surgical intervention it is of value preoperatively and postoperatively in many instances.

At present, Dr. William Saphir and I are studying the urinary excretion of anterior pituitary-like hormone in patients with endocrine cryptorchidism before and after treatment in an attempt to determine the physiology of cryptorchidism associated with dysfunction of the hypophysis.

VENTRICULAR PAROXYSMAL TACHYCARDIA IN A CHILD AGED THREE YEARS. DR. IRWIN RUBELL.

This article will appear in full in a later issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

Book Reviews

Diseases of the Endocrine Glands. By Dr. Hermann Zondek. Translated by Carl Prausnitz. Price, $11. Pp. 492, with 168 illustrations. Baltimore: William Wood & Company, 1935.

The author and translator of this book have made available to English-reading physicians an extremely interesting presentation of the subject of endocrinology. There is no sparing of detail, and indeed, it is the attention to detail, with a consideration of the meaning of apparently conflicting reports, that gives the book much of its soundness. That the action of the hormone depends largely on the physicochemical environment of the cells on which it acts explains many apparent contradictions. That this environment, in turn, is related to the activity of the vegetative nervous system and through the emotional phase to the central nervous system both broadens and complicates the study of endocrinology. Interhormonal activity, while a safeguard for the individual, is often a further source of confusion to the investigator and physician. To bring some sense of order to so complicated a field is no small achievement.

The first part of the book is given over to general considerations, including historical aspects, the mode of hormonal action, the interaction of hormonal glands, the physiology and chemistry of each gland and the relation of the endocrine glands to vitamins, to the vegetative nervous system and to the central nervous system. The last two chapters in this part have to do with methods for the examination of patients for endocrine disease and general remarks on organotherapy.

In the second part of the book Zondek discusses the pathology, etiology, symptoms and treatment of the following conditions: exophthalmic goiter, myxedema (congenital and infantile), endemic cretinism, tumors of the thyroid gland, tetany, obesity, cachexia hypophyseopriva and cerebropituitary emaciation, diencephalopathy, diabetes insipidus, precocious senescence, acromegaly, gigantism, dwarfism, osteomalacia, osteitis fibrosa, Addison's disease, hypermedullary adrenalism, hyperinsulinism, status thymicolymphaticus, diseases of the generative systems and pluriglandular insufficiency.

Growth: A Study of Johnny and Jimmy. By Myrtle B. McGraw, Ph.D. Cloth. Price, $3.50. Pp. 319, with 16 plates. New York: D. Appleton-Century Company, Inc., 1935.

This book records the results obtained from the study of the twins Johnny and Jimmy, which received considerable notoriety in the newspaper during the past year. The purpose of the investigation was to study the process of development as it is manifested in the growth of particular behavior patterns of the human infant and to evaluate the influence of exercise or use of an activity on its development.

Study was begun on the twins at birth. Johnny was taught various ontogenetic behavior activities, such as swimming, diving, ascending inclines, skating, manipulation of graded stools, manipulation of graded boxes and tricycling. These activities are illustrated by plates and are astounding as showing what can be accomplished by such a young infant.

At the end of the period of study the mental rating of the twins was 94 for Johnny and 91 for Jimmy. The author states: "Although Johnny had enjoyed earlier and more extensive practice in certain activities, he apparently was not greatly benefited thereby in the acquisition of performances of a different order. When achievement is measured by end results, his performances in most situations were not superior to those of Jimmy. . . Johnny was more inclined to pause and look the situation over before acting; he appeared more persistent and less willing to quit when he met with difficulty."

This bare recital of the results does not give at all an idea of the excellent unbiased material contained in this book. Each chapter contains a complete discussion of the processes involved and is intensely interesting. The book is well printed, and the plates are excellent.

Pediatric Treatment. By Philip S. Potter, A.B., M.D., F.A.A.P. Price, $5. Pp. 578. New York: The Macmillan Company, 1935.

This is a book on pediatric treatment. The first division deals with general pediatric therapeutic procedures, such as nursing, local applications, inhalations, injections, emergencies and pharmaceutics. The second division takes up the nutritional requirements of the child, and the third concerns diseases of the new-born. The final division includes the treatment of diseases by systems. The methods used in these treatments are standard and complete. An unusually good feature is the giving of complete prescriptions of drugs needed for the different age periods, and additional prescriptions are added in an extra chapter. There is no doubt that the writing of prescriptions has become a lost art in the last few years. The prescriptions given in this book should be of great value to the general practitioner or the young pediatrician.

Association pour le développement de l'hygiène maternelle et infantile. Siége social et administration. Pp. 65. Paris, 1935.

This publication includes a statement of the aims of the organization and includes a report by Weill-Hallé, the general secretary; the financial report by Jean du Pasquier, and the addresses given at the inauguration of the new buildings of the school of puericulture of the Faculty of Medicine of the University of Paris.

Annuaro de eststistica demographo-sanitaria 1927-28. Department nacional de saude pública, República dos Estados Unidos do Brasil. Paper. Pp. 131. Rio De Janeiro, 1934.

This volume contains in statistical tables the mortality in all types of disease, the age at death and the causes of death for the Republic of Brazil. It also includes the birth rate, the population of the provinces, and the hospital mortality. It is a very complete book for any one wishing these facts from this country.

Colwell's Daily Log for Physicians. By John B. Colwell, M.D. Price, $6. Champaign, Ill.: Colwell Publishing Company, 1935.

This record system for physicians is a duplicate of the one presented each year, this being the ninth annual edition. The record contains explanatory notes with daily pages for all the various entries that a physician would care to make. It is a useful article in any physician's office to help him keep up the business side of his profession.

Infant Nutrition. By Williams McKim Marriott. Second edition. Price, $4.50. Pp. 431, with 27 illustrations. St. Louis: C. V. Mosby Company, 1935.

In the second edition, printed five years after the publication of the first edition, a chapter on allergy has been added; the chapter on vitamins has been rewritten, and additions have been made in those on acidosis, alkalosis and anhydremia. The size has also been decreased by eliminating repetition. As to the subject matter in general, enough can hardly be said. It covers the field of infant nutrition thoroughly and interestingly. This is studied from a physiologic and practical standpoint. The discussion of practical feeding and of the nutritional disturbances is particularly excellent. In consideration of the welter of misinformation that has been published in the last few years, such a sane, practical book is much needed. It should be in every pediatrician's and general practitioner's library.

Directory of Pediatric Societies *

INTERNATIONAL

International Association of Preventive Pediatrics

President: Professor G. Scheltema, 6a Heereplein, Groningen, The Netherlands.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

FOREIGN

British Paediatric Association

President: Dr. Hugh Thursfield, 84, Wimpole St., London, W. 1.
Secretary: Dr. Arthur G. Maitland Jones, 31 A, Weymouth St., London, W. 1.

Royal Society of Medicine, Section for the Study of Disease in Children

President: Sir Lancelot Barrington-Ward, 85 Harley St., London, W. 1.
Secretary: Dr. K. H. Tallerman, 122 Harley St., London, W. 1.
Place: 1, Wimpole St., London. Time: Fourth Friday of each month, 4:30 p. m.

Paediatrický Spolok na Slovensku

President: Dr. A. J. Chura, Lazaretská 6, Bratislava, Czechoslovakia.
Secretary: Dr. S. Limbacher, Dlhá 2, Bratislava, Czechoslovakia.
Place: Pediatric Clinic, University, Bratislava. Time: Six times a year.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. Horton R. Casparis, Vanderbilt University Hospital, Nashville, Tenn.
Secretary: Dr. Ralph M. Tyson, 255 S. 17th St., Philadelphia.
Place: Kansas City, Mo. Time: May 11-15, 1936.

American Academy of Pediatrics

President: Dr. Henry Dietrich, 1136 W. Sixth St., Los Angeles.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.

American Hospital Association, Children's Hospital Section

President: Mr. Robert Witham, Children's Hospital, Denver.
Secretary: Miss Agnes O'Roke, Kosair Crippled Children's Hospital, Louisville, Ky.

American Pediatric Society

President: Dr. Fritz B. Talbot, 270 Commonwealth Ave., Boston.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid St., St. Louis.

Canadian Society for the Study of Diseases of Children

President: Dr. A. P. Hart, 1844 Bloor St., W., Toronto, Ont.
Secretary-Treasurer: Dr. Pearl Summerfeldt, Hospital for Sick Children, Toronto, Ont.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

SOCIETY FOR PEDIATRIC RESEARCH

President: Dr. C. F. McKhann, Children's Hospital, Boston.
Secretary: Dr. A. A. Weech, 3975 Broadway, New York.

SECTIONAL

NORTH PACIFIC PEDIATRIC SOCIETY

President: Dr. L. Howard Smith, 1020 S. W. Taylor St., Portland, Ore.
Secretary: Dr. Morris Bridgeman, Children's Clinic, Portland, Ore.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON PEDIATRICS

Chairman: Dr. Luther W. Holloway, 117 W. Duval St., Jacksonville, Fla.
Secretary: Dr. Madison Hines Roberts, 104 Ponce de Leon Ave., N. E., Atlanta, Ga.

STATE

ALABAMA PEDIATRIC SOCIETY

President: Dr. J. W. Britton, 931 Noble St., Anniston.
Secretary-Treasurer: Dr. Wallace Clyde, Employees' Hospital, Fairfield.

ARKANSAS STATE PEDIATRIC ASSOCIATION

Chairman: Dr. Morgan Smith, 625 Beech St., Little Rock.
Secretary: Dr. Madeline A. M. Melson, 2111 N. Spruce St., Little Rock.

CALIFORNIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

Chairman: Dr. S. J. McClendon, 2001 Fourth Ave., San Diego.
Secretary: Dr. Edward B. Shaw, 384 Post St., San Francisco.
Place: Coronado. Time: May 25-28, 1936.

GEORGIA PEDIATRIC SOCIETY

President: Dr. William Willis Anderson, 478 Peachtree St., Atlanta.
Secretary-Treasurer: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.
Place: Atlanta, December 1935. Savannah, June 1936.

INDIANA STATE PEDIATRIC SOCIETY

President: Dr. Louis H. Segar, 23 E. Ohio St., Indianapolis.
Secretary-Treasurer: Dr. Mathew Winters, 23 E. Ohio St., Indianapolis.
Time: Two meetings a year.

LOUISIANA STATE PEDIATRIC SOCIETY

President: Dr. Charles James Bloom, 3439 Prytania St., New Orleans.
Secretary-Treasurer: Dr. J. A. Crawford, 834 Ryan St., Lake Charles.

MEDICAL SOCIETY OF STATE OF NEW YORK, SECTION ON PEDIATRICS

Chairman: Dr. George M. Retan, 459 James St., Syracuse.
Secretary: Dr. John D. Craig, 33 E. 61st St., New York.
Place: New York City. Time: April 27-29, 1936.

MICHIGAN STATE MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. Edgar E. Martmer, 749 David Whitney Bldg., Detroit.
Secretary: Dr. C. R. Dengler, 131 W. Michigan Ave., Jackson.

MISSISSIPPI STATE PEDIATRIC SOCIETY

President: Dr. R. E. Wilson, 205 S. Harvey St., Greenville.
Secretary-Treasurer: Dr. Guy C. Jarratt, 920 Crawford St., Vicksburg.
Place: To be designated by Society. Time: Yearly.

NEBRASKA PEDIATRIC SOCIETY

President: Dr. J. A. Henske, 1614 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. J. H. Murphy, 915 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

NORTH CAROLINA PEDIATRIC SOCIETY

President: Dr. J. R. Ashe, 306 N. Tryon St., Charlotte.
Secretary: Dr. R. A. Moore, 306 N. Tryon St., Charlotte.
Place: Pinehurst. Time: May 6, 1936.

OKLAHOMA STATE PEDIATRIC SOCIETY

President: Dr. Julian Feild, 610 S. Monroe St., Enid.
Secretary: Dr. B. H. Nicholson, 301 N. W. Twelfth St., Oklahoma City.

PENNSYLVANIA MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. Joseph Stokes, Children's Hospital, Philadelphia.
Secretary: Dr. Theodore O. Elterich, 310 Medical Arts Bldg., Pittsburgh.

SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. William Weston Jr., 1428 Lady St., Columbia.
Secretary-Treasurer: Dr. Leland B. Salters, 317 S. Warley Ave., Florence.

TENNESSEE STATE PEDIATRIC SOCIETY

President: Dr. Joe T. Smith, 702 Medical Arts Bldg., Knoxville.
Secretary: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis.
Place: Memphis. Time: April 1936.

TEXAS PEDIATRIC SOCIETY

President: Dr. C. O. Terrell, 813 Medical Arts Bldg., Fort Worth.
Secretary-Treasurer: Dr. F. H. Lancaster, 1507 Medical Arts Bldg., Houston.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. Basil B. Jones, 1028 W. Franklin St., Richmond.
Secretary: Dr. W. A. McGee, 616 W. Grace St., Richmond.

WEST VIRGINIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

President: Dr. John T. Thornton, 58, 16th St., Wheeling.
Secretary: Dr. Claude L. Holland, 400 Locust Ave., Fairmont.

LOCAL

ACADEMY OF MEDICINE OF CLEVELAND, PEDIATRIC SECTION

Chairman: Dr. J. D. Pilcher, City Hospital, Cleveland.
Secretary: Dr. William M. Champion, 2323 Prospect Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

ACADEMY OF MEDICINE, TORONTO, SECTION OF PEDIATRICS

President: Dr. T. B. Verner, 170 St. George St., Toronto.
Secretary: Dr. D. V. Hutton, 170 St. George St., Toronto.

BRONX PEDIATRIC SOCIETY

President: Dr. Harry D. Pasachoff, 1560 Grand Concourse, New York.
Secretary: Dr. Samuel Tripler, 1555 Grand Concourse, New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

Brooklyn Academy of Pediatrics

President: Dr. W. F. Watton, 240 Berkeley Pl., Brooklyn.
Secretary: John A. Monfort, 861 Carroll St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Fourth Wednesday of each month, except May, June, July, August and September.

Central New York Pediatric Club

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Third Thursday of April and September.

Chicago Pediatric Society

President: Dr. A. Levinson, 30 N. Michigan Ave., Chicago.
Secretary: Dr. James H. Wallace, 715 Lake St., Oak Park, Ill.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month.

Dallas County Pediatric Society

President: Dr. I. T. Nesbitt, 1719 Pacific Ave., Dallas, Texas.
Secretary: Dr. John E. Ashby, 614 Medical Arts Bldg., Dallas, Texas.
Place: Bradford Memorial Hospital. Time: 1 p. m., first and third Saturdays of each month.

Detroit Pediatric Society

President: Dr. Edgar E. Martmer, 749 David Whitney Bldg., Detroit.
Secretary: Dr. W. J. Scott, 5140 Second Ave., Detroit.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. Joseph Yampolsky, 478 Peachtree St., Atlanta.
Secretary: Dr. T. I. Willingham, 384 Peachtree St., Atlanta.
Place: Academy of Medicine, 38 Prescott St., N. E. Time: Second Thursday of each month from October to April, 8 p. m.

Harris County Pediatric Society

President: Dr. Byron P. York, 3820 Fannin St., Houston, Texas.
Secretary-Treasurer: Dr. E. O. Fitch, 3717 Main St., Houston, Texas.
Place: Houston Club. Time: Third Monday of each month.

Intermountain Pediatric Society

President: Dr. Helmina Jeidell, 11 Exchange Pl., Salt Lake City, Utah.
Secretary-Treasurer: Dr. Edwin R. Murphy, 9 Exchange Pl., Salt Lake City, Utah.
Place: Salt Lake City, General Hospital. Time: First Thursday of each month. 8 p. m.

Kansas City (Missouri) Pediatric Society

President: Dr. Harry M. Gilkey, 1103 Grand Ave., Kansas City.
Secretary: Dr. S. A. Stadler, 6133 Brookside Blvd., Kansas City.
Place: Kansas City General Hospital. Time: On call.

Los Angeles County Medical Association, Pediatric Section

President: Dr. George P. Laton, 1136 W. 6th St.
Secretary-Treasurer: Dr. Edwin F. Patton, 3875 Wilshire Blvd., Los Angeles.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd.
Time: Second Monday of February, April, June, October and December.

MEDICAL SOCIETY OF THE COUNTY OF KINGS AND THE ACADEMY OF MEDICINE OF BROOKLYN, PEDIATRIC SECTION

President: Dr. Charles F. Fisher, 756 Eastern Parkway, Brooklyn.
Secretary: Dr. Harry Apfel, 988 Park Pl., Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: Third Wednesday of each month, October to May.

MEDICAL SOCIETY OF THE COUNTY OF QUEENS, INC., SECTION ON PEDIATRICS

Chairman: Dr. W. C. A. Steffen, 42 Union St., Flushing, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144, 38th Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

MEMPHIS PEDIATRIC SOCIETY

President: Dr. W. D. Mims, 1042 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. W. R. Graves, 1193 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month, except June, July and August, 8 p. m.

MILWAUKEE PEDIATRIC SOCIETY

President: Dr. J. Gurney Taylor, 324 E. Wisconsin St., Milwaukee.
Secretary: Dr. H. B. Miner, 425 E. Wisconsin Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. Paul Emerson, 319 Longwood Ave., Boston.
Secretary-Treasurer: Dr. Henry E. Gallup, 66 Commonwealth Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

NEW YORK ACADEMY OF MEDICINE, SECTION OF PEDIATRICS

Chairman: Dr. Béla Schick, 17 E. 84th St., New York.
Secretary: Dr. Alexander T. Martin, 107 E. 85th St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. E. F. Robb, 1801 Lyndale Ave., S., Minneapolis.
Secretary: Dr. A. V. Stoesser, University Hospital, Minneapolis.

PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. John D. Donnelly, 115 Bryn Mawr Ave., Bala, Pa.
Secretary: Dr. James E. Bowman, 4091 Comly St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

PITTSBURGH PEDIATRIC SOCIETY

President: Dr. George J. Feldstein, 3401 5th Ave., Pittsburgh.
Secretary-Treasurer: Dr. E. R. McClusky, 3200 Fifth Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Tuesday, alternate months from October to April, inclusive.

RICHMOND PEDIATRIC SOCIETY

President: Dr. Samuel A. Anderson Jr., 2326 W. Grace St., Richmond, Va.
Secretary-Treasurer: Dr. Emily Gardner, 1100 W. Franklin St., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: First Thursday of each month (except July, August and September).

ROCHESTER PEDIATRIC SOCIETY

President: Dr. F. W. Bush, 29 N. Goodman St., Rochester, N. Y.
Secretary: Dr. David Wolin, 16 N. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month.

ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. Ralph Verploeg, 1850 Gilpin St., Denver.
Secretary: Dr. Max M. Ginsburg, Metropolitan Bldg., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 2:30 p. m.

ST. LOUIS PEDIATRIC SOCIETY

President: Dr. J. V. Cooke, St. Louis Children's Hospital, St. Louis.
Secretary-Treasurer: Dr. Katherine Bain, Beaumont Bldg., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

SEATTLE PEDIATRIC SOCIETY

President: Dr. Arthur E. Wade, 1215, 4th Ave., Seattle.
Secretary: Dr. Walter B. Seelye, Cobb Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 6:30 p. m.

SOUTHWESTERN PEDIATRIC SOCIETY

President: Dr. Victor E. Stork, 1136 W. Sixth St., Los Angeles.
Secretary: Dr. Howard R. Cooder, 3875 Wilshire Blvd., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

UNIVERSITY OF MICHIGAN PEDIATRIC AND INFECTIOUS DISEASE SOCIETY

President: Dr. Daniel Budson, 3001 W. Grand Blvd., Detroit.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.

WESTCHESTER COUNTY MEDICAL SOCIETY, PEDIATRIC SECTION (NEW YORK)

President: Dr. Louis V. Waldron, 149 N. Broadway, Yonkers, N. Y.
Secretary-Treasurer: Dr. Fairfax Hall, 421 Huguenot St., New Rochelle, N. Y.
Place: Grasslands Hospital. Time: Third Thursday, Oct., Dec., Feb. and April.